

PATHOLOGICAL CHANGES OCCURRING IN THE ENDOCRINE
GLANDS IN CASES OF MENTAL DISEASE WITH
SPECIAL REFERENCE TO THE PITUITARY

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1. INTRODUCTION

The following thesis is concerned with the histological examination of some of the endocrine glands obtained from cases of mental disease; these have been compared with a series of glands obtained from cases of presumed normal mentality.

No special effort has been made to select any particular type of case. A certain number of senile cases have been included but the number has been reduced to a minimum.

The case protocols have been grouped under the appropriate mental headings; no diagnostic labels have been attached to cases; each case has been briefly described according to the salient points of its disordered mental reactions, and brief progress notes have been recorded.

A considerable number of the cases had been known to the writer during life and this fact helped to bridge the often inevitable gap between the laboratory and the bedside.

A striking caution was issued by Bucknell in the middle of the last century concerning the study of cerebral pathology; this applies equally well to any pathological investigation. He wrote: "It has been unfortunate for the cause of cerebral pathology that those writers who have devoted much care and attention to the observation of cerebral changes presented in

post-mortem examinations have either lacked the desire or the opportunity to make themselves acquainted with the mental phenomena which had preceded death. The careful and minute detail of appearances observed in the brains of persons supposed to have died insane, disconnected from any account of the symptoms which existed during life are of comparatively little value in the present imperfect state of pathological science."

It has always been the writer's endeavour in studying the reactions of both the sane and the insane to take account of the mental and physical factors involved and not to stress one at the expense of the other. The individual must be studied as a whole; every part is reacting to its own environment; each unit should be in harmony within the organism. Unit disharmony must react adversely to the whole.

To the writer this fact seems to be the keynote to the problem of human behaviour. In this essay one particular department of the organism has been studied and an effort has been made to demonstrate a lack of essential balance and to correlate this with its possible effect on the behaviour and reactions of the individual as a whole. The results have been summarised at the end of the Thesis.

As will be pointed out later, the histo-pathological approach to the problem of behaviour is beset with so many difficulties and generally confusing artefacts that

extreme caution is demanded if anything more than inference is expected. The dead and preserved cell is a vastly different structure from the living unit of protoplasm; certain information can be deduced as to the state of that cell during life but even this must be accepted with considerable reserve.

The biological approach must be a living one. It is the writer's hope to continue research into the ever fascinating problem of human conduct and to investigate the interaction of hormonal secretions in the living and if possible to correlate these with normal and abnormal reaction types of behaviour.

2. HISTORICAL

A brief historical survey of the glands of internal secretion is of interest and importance to all who wish to follow the growth of medical science during the past century.

Endocrinology is a precocious child, born about the middle of the last century, it has in the intervening years grown out of all proportions.

Thomas Addison² may fairly claim to have been the first man to describe an endocrine disease. In 1855 he described the disease which still bears his name and attributed its pathology to destruction of both suprarenals.

In 1882 and 1883 Kocher³ and Reverdin⁴ showed that

myxoedema was connected with the Thyroid gland.

In 1889, Brown-Sequard⁵ attracted world-wide attention to the new science by his communication to the Biological Society of Paris concerning the results of his experiment of injecting testicular juice into himself and noting its rejuvenating effect (he was 72 years of age at the time of the experiment).

In 1889 von Mering and Minkowski⁶ showed that the pancreas was at fault in diabetes mellitus. Schulze⁷, Ssobolew⁸, Oppie⁹ and others demonstrated the independence in the pancreas of the islets of Langerhans.

1886 is noteworthy as the year in which Pierre Marie¹¹ described what was the first well authenticated account of acromegaly and its relation to changes in the Hypophysis.

In 1906 Vassale and Generali¹⁰ discovered that the tetany produced by the removal of the thyroid was due to loss of the para-thyroid glands.

During the past 30 years there have been so many advances in the study of the ductless glands that only those of importance will hereafter be mentioned under the appropriate gland.

Prior to the middle of the last century there had been no scientific study of endocrinology. The effects of castration had been noted since antiquity, both in animals and humans.

Galen's 'humoral' theory is in some ways a dim fore-

runner of the modern science. Many of the prescriptions of medieval days contained extracts of animal matter - often in a crude and nauseating form.

Biedl¹² states that there were no less than 152 products of animal origin in apothecary shops in Innsbruck in the year 1765.

In recent years endocrinology has been more and more pressed into the realm of therapeutics, more often than not on purely empirical grounds. This unfortunate mistake has done a considerable amount of harm and has retarded rather than advanced this important branch of medicine.

The startling results of treating cases of myxoedema with thyroid and the equally brilliant results of insulin in diabetis have encouraged ambitious adventurers to try out the other commercial products of reputed standard; these have been given without any accurate knowledge of the supposed endocrine anomaly. The results have been, naturally, most erratic - an occasional brilliant cure - many dismal failures.

The symptomology of endocrine diseases is often remarkably obscure, due to our rudimentary knowledge of the subject and it will be a long time before we can hope for a completely rational basis of therapy.

3. THE PITUITARY GLAND

A. Anatomy.

This small but important gland is situated at the base of the skull; it is contained in a hollow portion of the sphenoid bone called the sella turcica. Its size and shape are variable; Schafer¹³ suggests about 9mm. in antero-posterior diameter, 6mm. in vertical measurement and 13mm. transversely.

The size of the sella turcica varies to a certain extent with that of the gland but it is possible to have a small pituitary in a large sella. The weight of the adult male gland is about .5gm. The female gland is heavier. Bucy¹⁴ quotes .57gm. for the average male adult when the dura and stalk have been removed. Falta¹⁵ and Schafer¹³ give half a gram. as the average male weight. Rasmussen¹⁶ gives the average as .56gm. (cases of accidental death in males).

Rasmussen¹⁶ notes an increase in weight roughly proportional to the height of the individual. Hatai¹⁷ noted an increase in weight which varied with the body weight, (in the rat).

Addison and Adams¹⁸ state that the entire gland is nearly double the weight in adult parous women than in men.

Erdheim and Stumme¹⁹ quote the following figures:
nulliperae - 61.8cgm. primiparae - 84.7cgm. multiparae - 106cgm.

Other factors causing enlargement and increase in weight are castration, myxoedema and sometimes in intracranial lesions.

The gland is invested by a layer of dura mater which is continuous with that covering the brain. Nacy¹¹ states that it is covered by all three meningeal layers.

The gland is attached to the brain by a stem like structure called the infundibulum - this is a prolongation of the tuber cinereum.

The gland when removed and cut through its long axis is found to be composed of two distinct parts - an anterior and larger part and a posterior and smaller and paler part; histologically it will be seen that the anterior part is highly cellular while the posterior part is made up chiefly of neuroglial tissue.

Developmentally the pituitary has a twofold origin. The anterior part is derived from the buccal ectoderm, being an invagination from the embryonal oral recess known as Rathke's pouch.

By constriction and isolation this becomes a vesicle which is transformed into the glandular structure and fuses with the posterior part.

The posterior part is derived from a central evagination from the diencephalon. The pars intermedia probably develops from the anterior lobe but this appears to be controversial and anatomically it appears to belong to the posterior lobe. Cushing²⁰ notes that on separa-

tion of the anterior lobe from the posterior lobe the pars intermedia always adheres to the posterior part.

It is to be noted that the anterior and posterior lobe are, in many animals separated by a cleft but that in man this cleft is usually obliterated or reduced to a series of cyst like spaces.

A further part of the gland is the pars tuberalis; this extends along the stalk over the tuber cinereum - this part is structurally and developmentally different from the main gland.

Bucy¹⁴ classifies the parts thus:

A.	Pars Bucalis)	Anterior lobe
	Pars anterior		
	Pars tuberalis		
	Pars intermedia		
B	Processus infundibuli)	Posterior lobe
	Infundibulum		

BLOOD SUPPLY The pituitary has an interesting vascular system. The anterior part of the gland has one of the richest blood supplies of any gland; the posterior lobe is singularly avascular.

The pars tuberalis is very vascular - the pars intermedia has few vessels.

The general blood supply comes from the circle of Willis and from the internal carotids. The arterioles converge and pass along the stem; most of them passing to the anterior lobe; some vessels leave the stem and supply the posterior lobe; in addition there is a special

median artery derived from the internal carotids which terminates in the pars nervosa (Schafer¹³).

Recently Popa and Fielding²¹ have worked out a vascular link between the pituitary and the hypothalamus; they show that there is a system of vessels which collects blood from both lobes of the pituitary and distributes it to the hypothalamus; this has an important bearing on the recent work of Cushing^{21A} on the relation of the pituitary to the hypothalamus.

Lymph spaces probably do not exist in the pituitary. Caselli²² described their presence in the anterior lobe but others failed to find them - Herring²³ noted lymph channels in the pars intermedia but Hughson^{23a} thinks these are probably compartments in the subarachnoid space.

NERVE SUPPLY Little definite is known on this subject. Dandy²⁴ reports the presence of sympathetic fibres from the carotid passing to the anterior lobe along the arteries; a few fibres go to the posterior lobe, and one to the pars intermedia. These fibres are non-myelinated and probably only go to the arteries. Myelinated fibres are reported to have been seen and these ended by ramifying over the cells of the anterior lobe (Thaon²⁵).

Large tracts of fibres have been seen arising in the nucleus supraopticus in the floor of the third ventricle and descending through the tuber cinereum

down the stalk into the infundibular process; after this they are said to spread out fan-wise and terminate in large end bulbs; Tello²⁶ thinks these may be the bodies which are sometimes thought to be colloid or hyalin bodies (Bucy¹⁴). These fibres are only seen when the preparation is stained with Cajals Silver Pyridine stain.

The Golgi apparatus in basophils is directed towards the blood-vessels while that of the eosinophils is towards the centre (Cowdry²⁷) Reiss²⁸.

B. Histology

Pars Anterior. Cells are of two main types:
Chromophobe,
Chromophil.

The chromophobe cells have no affinity for dyes and their cytoplasm remains unstained or at the most becomes faintly coloured. The nuclei of these cells stand out with great clarity and are very conspicuous in most glands examined under the higher powers.

Synonyms for these cells are: Chief cells; reserve cells; undifferentiated cells; neutrophils. According to Erdheim and Stumme²⁹ these develop into the so-called pregnancy cells.

The chromophils are divided into:
Eosinophils (Oxyphils: acidophils)
Basophils.

Eosinophils stain with the acid dyes - eosin and acid fuchsin. They are usually coarsely granular and

stain well. Recently it has been suggested that the acid staining granules should be called Alpha granules (Davidoff and Bailey³⁰) and the basophils Beta granules.

Basophils stain with the basic dye haematoxylin. The granules in these cells are not as marked as those in the acidophil or eosinophil cells.

In addition to the above mentioned main types there is the undifferentiated epithelial cell; this is practically the only type of cell found in the foetal gland and from this the other cells are developed. It has recently been pointed out by Cooper³¹ that there can be found in many glands small masses of these undifferentiated cells.

The oxyphils are the first to be differentiated and are present at the third month of foetal life. During childhood they increase rapidly until puberty when they form almost one-half the total number of cells in the anterior lobe (Cooper³¹). They decrease after the fiftieth year. The nucleus is well stained and usually stands out clearly and has a well marked nucleolus.

Eosinophil cells are increased in and after pregnancy - they increase in size and become even more granular. They are greatly increased in acromegaly, frequently forming adenomata. It has been noted that they are increased in diabetes mellitus (Fry³²); Kraus³³ however notes diminution of oxyphils in this case.

The basophil cells become differentiated a little later than the oxyphils; normally the basophils are never as numerous as the oxyphils (Cooper³¹). They multiply much more slowly but, in contrast to the oxyphils they increase until old age. In shape the basophil is a large cell, the cytoplasm being finely granular and usually staining deeply; the nucleus stains deeply but is often obscured by the depth of stain of the cytoplasm. During oestrus the basophils are increased in number (Rasmussen).

The chromophobe cells present the most variable picture; they are usually very numerous and frequently exceed the oxyphils; Rasmussen³⁴ estimates their number as 50% of the total cells in the anterior lobe. Mature chromophobes are large and angular with scanty unstained cytoplasm (slightly granular); the nucleus is not stained deeply with the usual haematoxylin stain though this stain brings out the chromatin and the nucleolus. The chromophobe cells appear to increase with age. They increase together with the oxyphils, in pregnancy.

Erdheim and Stumme²⁹ consider that the chromophobes are poor in lipoids, while the chromophils contain large quantities. Chromophobes are often found invading the pars intermedia and the posterior lobe.

The Relative numbers of the three types of cell in the anterior lobe.

On this question there is a great diversity of opinion. If Blair Bell's³⁵ theory of the relation of the cells is accepted (see below) then the highest percentage of any particular type would depend on the functional state of the gland at the time of death or removal; this would naturally vary considerably from one case to another.

Cooper³¹ found in her series of cases that the oxyphils easily predominated in early adult life but that as age advanced the numbers tended to become equal, with a slight predominance of oxyphils.

Ramussen³⁴, as mentioned before, gives the relations as:-

Chromophobes	50%
Oxyphils	37%
Basophils	11%

Kiyono^{35a} finds basophils preominate. Thom³⁷ states that eosinophils make up one third of the total number. In my own studies the numbers varied considerably and only by cutting serial sections of not more than 8 microns thickness could any degree of accuracy be secured.

Relation of Types to each other.

There are two schools of thought on this question. Schafer¹³, Blair Bell³⁵, Saint Remy³⁶, Benda³⁷ and others believe that the chromophobe and chromophil cells represent the same structure at different stages of activity.

Gemelli³⁸ and Erdheim³⁹ believe that these cells are quite different and have their own secretions.

Blair Bell³⁵ believes that the eosinophil cell represents the normal actively secreting stage (discharging secretion into the blood-vessels or lymphatics). If there is no great demand for secretion many may enlarge and become basophil; these then gradually enlarge and swell and discharge basophil colloid and then become small and shrunken and faintly staining (chromophobe cells). When there is an immediate demand for secretion these chromophobe cells regenerate into larger chromophobe cells and eosinophilia - a more leisurely process - does not occur (e.g. in pregnancy and after thyroidectomy). Schafer concludes that there is little doubt that oxyphil and basophil granular cells are derived from and may revert to chromophobe cells but once formed they do not undergo transformation but develop along diverging lines.

Cooper³¹ from her developmental and consequent studies concludes that the oxyphils originate first (from the undifferentiated cells); from these oxyphil cells the basophils are formed. After discharging their secretion they appear as neutrophils and from these neutrophils or chromophobes arise oxyphils and basophils again. This sequence is represented as:- eosinophil - basophil - neutrophil - eosinophil - etc.

Fraser⁴⁰ holds that the primary cell is the basophil.

Pars Intermedia.

This is the smallest part of the pituitary. It is composed of a layer or two of cells situated on the posterior side of the cleft and is practically attached to the posterior lobe. In some of the lower animals (e.g. cat) it is a much deeper structure. The cells are mostly basophil. The writer finds eosinophil cells much more commonly present in the pars intermedia but they lack the pronounced granules of the anterior lobe basophils; these cells tend to form vesicles and it is common to find these vesicles filled with colloid (usually basophil but sometimes oxyphil).

There are usually some chromophobe cells and these tend to invade the posterior lobe.

Herring⁴¹ describes globular masses of colloid sometimes of a hyaline nature; these are traceable through the posterior lobe.

The blood supply is poor and there are no blood sinuses as in the anterior lobe.

The Posterior Lobe.

Often referred to as the pars nervosa or neurohypophysis, this lobe is composed of neuroglial fibres with a variable number of glial cells scattered throughout. There do not appear to be any nerve cells and until recently it was thought that there were no nerve fibres. (Herring⁴¹).

More recently (1925, 1927) Pines⁴² and Greving^{42a} have described large tracts of nerve fibres arising from the nucleus supraopticus in the floor of the third ventricle, descending through the tuber cinereum and spreading out fan-wise in the posterior lobe. These fibres terminate in end-bulbs which have a densely reticulated appearance. Tello²⁶ suggests that these end bulbs may be the hyalin bodies which are so commonly observed. It is to be noted that the nerve tracts referred to can only be demonstrated by Cajals silver-pyridine stain.

Bucy¹⁴ has made a careful study of the glial cells of the pars nervosa and has suggested the name Pituitocytes for them. He used the silver-carbonate technique for this work. The following is a brief description of these cells. They vary in size and shape. The cytoplasm is irregular, and the nuclei are not constant in their appearance - the chromatin is often diffuse and there is no nucleolus. Each cell has a process extending for a long distance (these processes are a good deal longer than any other glial processes). The cells may be uni- or bipolar. The processes referred to terminate in the connective tissue of blood vessels or of the fibrous septa which run into the lobe.

Pigment.

A dark, yellowish brown pigment is frequently found scattered throughout the posterior lobe. It occurs in

the glial cells themselves and in the spaces between them (also in the ependymal cells which are sometimes seen). Vogel⁴³ thinks it is a product of the metabolism of the lobe; he also states that it is not melanin nor of a lipoid nature. It does not contain iron. Kohn⁴⁴ notes that it is increased in old age. Stendell (1913)⁴⁵ and Schonig (1926)⁴⁶ thought this pigment originated from basophils which had invaded the posterior lobe (Bucy¹⁴ thinks this is very unlikely). There is some evidence that it may be a lipo-fuscin as it is similar to the pigment found in the intestinal wall in pseudo-melanososis (Wells⁴⁷). Fischer⁴⁸ thinks it is a senile degenerative process.

Colloid masses are frequently found scattered throughout the lobe. Herring⁴¹ was the first to notice these and he concluded that they represented the secretion of the pars intermedia passing through the posterior lobe on its way to the third ventricle and so into the cerebro-spinal fluid. (See discussion on paths of secretion).

The cleft which separates the posterior lobe (with the pars intermedia) from the anterior lobe is the remains of the cavity of the pouch of Rathke. The cleft is wide and well defined in uterine life and childhood; after puberty it narrows and about thirty it has usually ceased to exist (cf. pathological descriptions). As the cleft narrows there appear masses of colloid, often in vesicles - these probably represent the secretion

of the pars intermedia cells. Fraser⁴⁰ has studied the appearance of the cleft in childhood and notes considerable variation in the amount of colloid matter seen. This colloid usually stains basophil and is often greatly increased in old age. The cleft is not infrequently seen in old subjects and may be caused by shrinkage of the anterior lobe.

The infundibulum or stem connects the hypophysis to the brain. It is short and funnel shaped. The cavity of the stalk is closed where it enters the posterior lobe but in some animals the cavity is continued down through the posterior lobe (e.g. cat).

There is no sign of any activity in the stalk; it is composed of neuroglial tissue which is continuous with that of the posterior lobe. Many blood vessels pass up and down the stalk from the gland.

Pars Tuberalis.

This is the part of the gland which extends forward over the base of the brain, its cells are basophil and there is usually a good deal of colloid which often occurs in vesicles. The vascularity is well marked and is almost as great as that of the anterior lobe.

C. PHYSIOLOGY AND MODE OF SECRETION OF THE PITUITARY

It is, naturally, in the realm of physiology that the greatest advances have been made in endocrinology in recent years.

Of all the ductless glands the pituitary has probably received more study than any other and despite a considerable accumulation of facts and a wealth of speculation there remains quite an alarming amount of ignorance on its true mode of function. It seems fairly well established that the secretion of the anterior lobe is poured directly into the blood stream.

The problem of the secretion from the pars intermedia (with or without some modification from the posterior lobe) and its absorption has not yet been definitely settled.

Two somewhat opposed views are still held. Firstly is the assumption that the secretion from the pars intermedia passes through the pars nervosa and the infundibulum and so into the cerebro-spinal fluid. This view was put forward first by Herring⁴¹. He noted the presence of colloid and hyalin masses apparently passing through on their way to the third ventricle (Haliburton, Candler and Sikes⁴⁹). Cushing and Goetsch⁵⁰ gave further confirmation to this theory by showing that the cerebro-spinal fluid possessed the same active principles as an extract from the posterior lobe. Later Dixon⁵¹ verified this by the uterus test.

Others whose views coincide with Herring's are: Schafer¹³; Trendelenburg⁵²; Oehma⁵⁴; Mayer⁵³; Miura⁵⁵.

Carlson and Martin⁵⁶ (1911) and Jacobson⁵¹ (1920) discounted the results of Cushing and Goetsch by showing that artificially prepared spinal fluid containing only organic salts could produce the cardio-vascular and diuretic effects ascribed to the posterior pituitary extract. In 1922 Maure and Lewis⁵⁸ postulated a vascular route of absorption. Hogben⁵⁹ demonstrated that the secretion is blood-born in amphibia (1924). McLean⁶⁰, using the uterus and melanophore assays, adduces evidence that presumptive pituitrin is present in canine, bovine and human blood plasma and cerebro-spinal fluid and that it is probably absorbed solely by a vascular route.

Van Dyke, Baily and Bucy⁶¹ also support a vascular theory of absorption.

Blair Bell⁶³, who was an advocate of the passage of the secretion into the cerebro-spinal fluid, suggests that the secretion may be modified through its contact with the substance of the posterior lobe.

For descriptive purposes it is customary to discuss the properties of the secretions of the pituitary gland under the two separate headings: anterior lobe secretions and posterior lobe secretions (the latter including the pars intermedia). This separation may be wrong; Blair Bell⁶³ considers that we should regard the pituitary as

one organ. In practice there is no doubt that it is the exception to be able to show specific involvement of one without some accompanying change in the other.

Anterior Lobe.

Following the discovery that enlargement of the anterior pituitary lobe coincided with increased growth of the body a large number of experiments were conducted in this field. (Goetsch⁶⁴, Schafer¹³, Sisson and Broyles⁶⁵ and more recently Evans and Long⁶⁶). All these experiments demonstrated an increase in body growth after more or less prolonged administration of anterior pituitary extract.

Cushing⁶⁷, Crowe and Homans⁶⁷ tried experiments with transplants - these were only partially successful as most of the transplants failed to develop. At the same time it was noted that posterior lobe extracts had a retarding effect on growth. My own experiments on mice bore out these conclusions.

The results of extirpation have been recorded by many observers among whom may be mentioned Cushing²⁰, Blair Bell⁶³, Biedl¹² and Paulesco⁶⁸. Total removal causes death. (Sweet and Allen have succeeded in removing the whole gland from a dog without death ensuing). Partial removal of the anterior lobe causes atrophy of the sexual organs: deposits of fat: defects of bone growth and lack of sexual power. If the stalk is damaged similar results follow (Paulesco) due, of course

to the blood supply being cut off and with it the secretion.

Camus and Roussy⁶⁹ consider the hypophysis is not essential to life. They think that the fatal results of extirpation experiments are due to damage to the brain caused by the operation.

Recently considerable work has been done on the relation of the anterior pituitary hormones to the sexual cycle. Some connection had been recognised for a long time and it had been noted that ablation of the anterior lobe or part of it had produced changes in the testicles and ovaries and alterations of the sexual power. Evans and Long⁶⁶ in their experiments on rats noticed that in the giant rats they produced the ovaries were twice as heavy as the control and many showed substantial corpora lutea but ovulation and oestrus did not occur.

Aschheim and Zondek⁷⁰ found that minute transplants of macerated anterior substance into immature mice produced precocious ovarian activity - ovulation, corpus luteum formation and oestrus.

These apparently contradictory findings seem to show that there must be two active principles in the anterior lobe. Evans and Simpson⁷¹ believe there are two distinct and separate sex hormones produced by the anterior pituitary.

Smith and Engle⁷² and Engle⁷³ also found that

anterior pituitary transplants caused follicular development and superovulation.

At about the same time came the announcement by Aschheim and Zondek⁷⁴ that the urine of pregnant women contained this luetinizing substance.

Aschheim and Zondek⁷⁵ have claimed to have obtained the two hormones separately by preparing them from different sources. The follicle stimulating hormone called by Zondek, Prolan A was extracted from the urine of women in the menopause or after ovariectomy; this extract produced stimulation of follicles with ripening and ovulation (in mice). The luetinizing hormone called by Zondek, Prolan B was prepared from anterior pituitary lobes; this extract produced luetinization of follicle walls with the formation of corpora lutea and consequent imprisonment of the ova.

It has been suggested by Kestner, Liebeschutz-Plaut and Schadow⁷⁶ that there is a pituitary hormone responsible for the specific dynamic action of foods.

This question was investigated by Foster and Evans⁷⁷ who verified the conclusions of the German workers. They also found that the loss could not be replaced by glandular therapy but that transplantation of either anterior or posterior lobe restored the specific dynamic action of the glycocoll injections used.

Foster and Smith observed atrophy of the thyroid in rats whose pituitaries had been removed. Crew and

Wiesner⁷⁸ have also brought forward evidence of the existence of a thyreotropic hormone in the anterior lobe of the pituitary.

Lee and Gagnon⁷⁹ noted a decrease in the metabolic rate in rats which were receiving daily injections of anterior pituitary - and which were showing increased weight. The assumption is that the growth hormone may stimulate anabolism and inhibit catabolism (Bugbee, Simond and Grimes⁸⁰).

Teel observed an increased water exchange in dogs which were receiving daily injections of growth hormone (action may be non-specific).

Frie, Stricker and Grueter⁸¹ noted increased mammary development and abundant lactation in animals receiving anterior pituitary hormone; corroborative work has been done by Corner⁸².

Teel and Watkins⁸³ have demonstrated a decrease in non-protein nitrogen following the injection of alkaline beef extracts of anterior pituitary.

The above mentioned reported functions of the anterior pituitary have been concisely summarised by Bugbee, Simond and Grimes⁸⁰ as follows:

1. Stimulation of growth.
2. Stimulation of sexual development and ripening of follicles.
3. Stimulation of lutein cells - preventing ovulation.
4. Stimulation of sexual development by a substance which can be administered by the mouth.
5. Increasing the specific dynamic action of foods.

6. Stimulation of thyroid.
7. Lowering of metabolism (gaseous).
8. Stimulation of water intake and output.
9. Stimulation of lactation.
10. Lowering of blood non-protein nitrogen.
11. Initiation of menstrual bleeding.

Hartman, Firor and Geiling⁸⁴ were responsible for the discovery that there is an anterior hormone responsible for the onset of the bleeding of menstruation.

So far we have no knowledge of how many separate chemical substances are responsible for these diverse actions; it is unlikely that there is a specific one for each action.

Two of these hormones have been chemically separated and roughly identified. The growth hormone is quickly and completely destroyed by the action of .4% tricresol; the sex hormone is uninjured by this strength of the same substance (Bugbee, Simond and Grimes⁸⁰).

Both hormones are quickly destroyed by weak acids but can be kept for some days in weak alkaline solutions. Both are destroyed by slight elevation of the temperature. Both can be salted out from glandular extracts by means of 20% sodium sulphate; this may indicate that they are absorbed by proteins.

Brailsford Robertson⁸⁵ isolated a substance from the anterior lobe to which he gave the name tethelin; this he found was present in alcoholic extracts and he considered it to be the growth promoting hormone. He also called attention to the fact that it accelerated healing in experimental wounds.

These observations have been repeated by other workers - Drummond and Canaan⁸⁶ - who obtained negative results.

Aschheim and Zondek Pregnancy Test

First published in 1928 this test has been investigated by many workers and its accuracy has been thoroughly tested. The test depends on the increased production of anterior pituitary hormone and its resulting presence in the urine of pregnant women.

The presence of this substance is detected by injecting the urine into immature mice or other animals, and noting the luetinizing action on the ovaries.

Technique. The original procedure was to inject about five immature female mice (about 3-4 weeks old and weighing about 7gms.) with 3 ccm. of urine twice daily for three days - the urine being a fresh specimen each time. On the fifth day the animals were killed and the ovaries examined; the presence of corpora haemorrhagica or corpora lutea being taken as diagnostic of pregnancy. Any changes in the uterus or vagina must be discounted as these are due to the presence of oestrin in the urine.

Other methods employ the rabbit and the urine is injected intravenously in larger amounts - 6ccm. - but only twice.

The test has been positive as early as the fifth week of pregnancy.

Recently Fluhmann⁸⁷ has published a series of cases in which he has been able to demonstrate the presence of the two sex hormones in the blood of non-pregnant women.

The procedure is to inject 5ccs. of blood serum from the patient into immature mice and later examine the ovaries.

The finding of mature graafian follicles is considered proof of the presence of the follicle ripening hormone (APH-A).

Lutenized cysts or luetin cells denoted the presence of the luetinizing hormone (APH-B).

The test should be negative in women with a normal 28-day menstrual cycle. If there is much ovarian failure the test is positive.

Posterior Lobe (including pars intermedia).

As long ago as 1894 Oliver and Schafer⁸⁸ demonstrated that extracts of pituitary had a blood pressure raising effect in some ways akin to that supra-renal extract.

Dale⁸⁹ discovered the specific action of pituitrin on the plain muscle of the uterus.

Blair Bell and Hick⁹⁰ noted the effect of the extract on the small intestine.

Ott and Scott⁹¹ and Schafer and Mackenzie⁹² recorded the galactogenic action of posterior pituitary extract; Schafer attributes this to contraction of the

plain muscle of the mammary gland and not to any increased production of milk.

Magnus and Schafer⁹³ showed that the extract caused dilation of the renal vessels and increased output of urine. It should be noted that intravenous injections cause the diuresis (after an initial diminution) but subcutaneous or intramuscular injections produce a diminution of output (especially if there has been a polyuria).

The diuretic action was regarded by Schafer and Herring as due to a direct action on the renal cells. The anti-diuretic action they assumed might be due to some regulation of the amount of water absorbed by the tissues.

The effects of posterior pituitary injections on metabolism have received a certain amount of attention. Thompson and Johnston⁹⁵ noted a stimulating effect.

Hewitt noted an increased elimination of ammonia in the urine.

Goetsch, Cushing and Jacobson⁹⁶ noted emaciation after repeated injections in dogs.

Carbohydrate metabolism is directly affected by posterior lobe injections. This fact was first noted by Borchardt⁹⁷ in 1914.

Injections cause a lowering of carbohydrate tolerance and glycosuria.

Colwell, A.R. (Medicine, vi, 1-39) (1927) considers

that the question of the action of the pituitary in carbohydrate metabolism is far from settled. He inclines to the idea that it is not an internal secretion from the hypophysis that is important but that there are nervous pathways or centres near the hypophysis which control carbohydrate metabolism and that these, being upset, produce the diabetic condition not infrequently seen in acromegaly.

Cushing²⁰ noticed that after injections in dogs there was a rise in body temperature; this has been further demonstrated by Rogers⁹⁸.

The pigmentary function of the posterior lobe has been studied by Hogben⁹⁹; it was found that removal of the posterior lobe of the frog caused it to become and stay pale - the melanophores lost their pigment. This effect on pigment has recently been used as a delicate assay for the presence of pituitrin (McLean).

Recently Bugbee and Kamm¹⁰⁰ have isolated two active and distinct principles from posterior lobes. The oxytocic substance which stimulates contraction of the uterus and which has been named Alpha-hypophamine. The pressor principle, called Beta-hypophamine, which raises blood-pressure. This pressor substance stimulates peristalsis in the gastro-intestinal tract; has both diuretic and anti-diuretic actions and causes expansion of the melanophores of the frog.

The posterior pituitary has some influence on fat

metabolism. Cooper and Chamberlain¹⁰¹ noted that injections caused a rapid increase in liver fat. Raab¹⁰² noted the same and that the blood fat was reduced after injections.

Conditions of hypofunction of the posterior lobe are associated with the deposition of fat especially of the so called girdle distribution. (103).

The recent work of Harvey Cushing^{21a} (Pituitary body. Hypothalamus and Parasympathetic Nervous System. 1932) has thrown fresh light on the mode of action of the neurohypophysis and has produced a complete alteration in our concepts of the dynamic action of this part of the pituitary gland.

The mode of escape of the secretion of the posterior lobe is considered to be twofold - into the C.S.F. through the infundibulum, and via the blood stream (following the route worked out by Popa and Fielding²¹).

The action of pituitrin when introduced into the circulation is well known and has been extensively studied. Cushing finds an entirely different action to result from the introduction of pituitrin directly into the third ventricle. His results were obtained and verified as the result of several carefully worked out experiments on patients whom he had operated on for the removal of various intra-cranial tumours. Briefly the results are as follows:

Pituitrin introduced into the human ventricle

produces flushing, sweating, salivation, lachrymation, vomiting and pronounced fall of body temperature. These results are very similar to those associated with parasympathetic stimulation.

Pilocarpine introduced into the ventricle produces a similar action.

As is well known the results of introducing pituitrin into the bloodstream are vaso-constriction - causing pallor - and stimulation of the lower bowel (sympathetic action).

Both the action of pituitrin and pilocarpine are counteracted by atropine, whether given subcutaneously or intraventricularly. Avertin (tribrom-methanol) checks the action, presumably by its elective action on the midbrain centres. The action of intraventricular pituitrin is abolished in cases of hydrocephalus where the tuberal portion of the midbrain is thinned out or where it is the seat of a tumour.

It has been shown (Greving, Pines⁴²) that there is a large tract of unmyelinated nerve fibres passing from the supra-optic and paraventricular nuclei and ramifying widely throughout the neurohypophysis. These appear to innervate the cells of the pars intermedia (Pines).

It has been shown by Karplus and Peczenik¹⁰⁹ that stimulation of the tuber electrically produces an increase of

the oxytocic and melanophore-expanding substance in the c.s.f.

It is also known (Hoff.H. and Wermer,P.¹¹⁰ Arch. exptl.Path.Pharmakol.cxxxiii,84-102, 1928) that emotional stimuli increase the amount of pituitrin in the c.s.f.

The working concept assumed from these data is that under emotional stimuli there is a discharge of secretion from the neurohypophysis (via nervous pathways through the tubero-hypophysial system); this secretion finds its way into the c.s.f. (probably directly and via the known vascular route) and by diffusion through the ependyema comes to act on the parasympathetic centres of the diencephalon.

Under certain conditions there may be sufficient discharge of posterior pituitary hormone to produce a diffuse parasympathetic response comparable to that of adrenalin in its relation to the sympathetic.

Finally that the neurohypophysis may bear the same relation to the parasympathetic that adrenalin does to the sympathetic.

The action of intraventricular pituitrin has been criticised by Abel who considered that the reactions produced were due to small amounts of histamine present in the extracts used. This criticism was put to the test by (1) injecting histamine intraventricularly and noting that the result was in no way comparable to that

of pituitrin. (2) Obtaining extracts which were carefully examined and passed as free from any histamine. This produced the same effects.

D. PATHOLOGY OF THE PITUITARY GLAND

Much has been written on the pathology of the Endocrine glands and in particular on the Pituitary. Cushing²⁰ and Blair and Bell⁶³ have devoted a book each to the subject and the number of articles published is enormous. Excellent accounts are given in the works of Engelbach and Tierney¹⁰⁴, Biedl¹², and Falta¹⁵ and in *Endocrinology and Metabolism*. Only a brief summary of the more important points will be attempted here.

Where possible, departures from the normal working of a gland are described in terms of over or under function - hyper or hypo function. This simple distinction is ^{now} ~~is~~, however, always possible; it may happen that the gland has several functions, possibly opposed to themselves; in these cases the resulting signs and symptoms cannot usually be directly classified as either increased or decreased function of the whole gland and it is necessary to describe the part of the gland which is over or under functioning.

Sometimes there is complete masking of the final result of the interacting processes and the only description which can then be applied is dysfunction of the whole gland. This last group is perhaps in some ways the most important clinically. Clear cut cases of hyperpituitarism are relatively rare and cases of hypopituitarism are even rarer. Undoubtedly cases

where the two lobes are at different functional levels are much more common in the general collection of clinical material (dysfunctional group).

Hyperpituitarism.

Two clinical types are commonly described. Acromegaly, in which the over-activity develops after the epiphyses have united and Gigantism, in which the over-activity starts before the epiphyses have united; the latter condition produces uniform enlargement of the long bones resulting in excessive stature.

In Acromegaly the bony overgrowth is more or less localised to certain parts: the lower and upper jaw and the malar bones; the hands and feet and the vertebral column (causing kyphosis).

Increased sexual excitement occurs (due probably to stimulation of the basophil cells). There is marked connective tissue hyperplasia causing enlargement of the lips, nose and tissues of the hands and feet. Sweating is sometimes marked. Glycosuria is variably present and is related to changes in the posterior lobe.

Hair growth is not infrequently involved - excessive growth on the trunk and extremities is common; the eyebrows may thicken and in the female there may be growth of hair on the face and chin.

Menstrual disturbance is the rule in women and sooner or later amenorrhoea occurs. The female may

develop masculine characteristics and there is an increased activity of the interstitial cells. Progressive weakness is almost invariable.

In the course of the disease the state of activity gradually gives place to one of hypoactivity and in this stage the sexual appetite and power are lost.

Other signs and symptoms may occur and are usually due to alterations in the other endocrine glands.

In addition to the above changes which are due to the altered secretion of the pituitary gland there are important symptoms referable to the pressure effects of the tumour: these are headache, eye signs (choked discs, enlarged blind spots, yellow discs and contracted visual fields), vertigo, tinnitus and deafness.

Fritsche and Klebs¹¹¹ appear to have been the first to describe enlargement of the pituitary body in gigantism (Ein Beitrag zur Pathologie des Riesenwuchses. Leipzig 1884, F. C. W. Vogel). Minkowski¹¹² in the same year suggested that the pituitary might be related to acromegaly (Berl. klin. Wchnscher, 1887 xxiv, 317). In 1886 Pierre Marie definitely associated the pituitary with acromegaly; he thought, however, that the tumour acted by destroying the functioning glandular tissue. Tamburini¹¹³ described a series of cases (Riv. sper. diffreniat. 1894, xx, 559 and xxi, 414, 1895) and he considered that the condition was one of hyperfunction (Benda and others also upheld the hyperfunctional theory).

Although the causation of acromegaly with its associated hyperfunction of the anterior lobe of the pituitary, has been recognised for some time it is comparatively recently that the hypofunctional conditions came to be recognised. Frolich¹¹⁴ was the first to describe a case in 1901 (Tumor der hypophyse ohne Akromegalie. Wien. klin. Rundschau, 1901, Nr. 47, 48). Since then many other cases have been described and the types referred to came to be differentiated. Paulesco¹¹⁵ in 1907 removed the pituitary from dogs and described the results under the name of cachexia hypophyseoprivia - a condition characterised by weakness, loss of weight and death (L'Hypophyse du Cerveau. Vigot Freres, Eds., Paris 1908). In 1914 Simmonds¹¹⁶ described a clinical case which corresponded to the findings of Paulesco in the dogs whose pituitaries he had removed. Pathologically this case showed necrosis and scar tissue in the anterior lobe of the pituitary. Clinically there was a condition of premature senility with marked muscular weakness and attacks of unconsciousness. Besides the changes in the pituitary there was atrophy of the kidneys, ovaries, pancreas and liver (Deutsche, med. Wchnschr xl, 322, 1914). As previously stated several other workers attempted to remove the pituitary but the results were divergent, probably on account of the difficulty of ensuring complete removal of the gland or rather the anterior lobe.

It was found that after experimental removal of the anterior lobe there was a rapid involution and sometimes degeneration of the thyroid and gonads. It was also noticed that adiposity was a common accompaniment, and this was at first attributed to the actual removal of the anterior lobe; later experiments (Camus and Rousy¹¹⁷ - Compt. rend. soc.de.biol. lxxxiii, 1578, 1920 and Endocrinol. iv, 507, 1920) demonstrated that the fatness was due to injury to the tuber cinereum; Erdheim¹¹⁸ had previously suggested this (Sitzungsber.d.k. Akad. d. Wissensch.Math. - naturw. Cl.,Wien, cxiii, 537 1904).

P. E. Smith¹¹⁹ was able to separate the two conditions of cachexia hypophyseopriva and dystrophia adiposa-genitalis and to allot a special pathology to each. The former condition resulted from total ablation of the anterior lobe of the pituitary while the condition of atrophy of the genitalia with adiposity was constantly associated with injury or lesions to the tuber cinereum (J.A.M.A. 88, 158, 1927). It should be noted however that in the light of the recently reported close association of the tuber cinereum and the hypothalamic centres to the pituitary that it may not be correct to rigidly dissociate these two syndromes.

A very comprehensive article on anterior pituitary insufficiency (Simmonds disease) appeared last year (Bull, John Hop, hosp. 50, 87, 1932). In this there

is a summary of most of the cases reported in the literature on the subject. The symptomology, as described in this paper, is as follows: progressive emaciation with changes in the integument - falling out of the teeth and hair (especially in the axillary and pubic areas) trophic changes in the nails and loss of lustre of the skin, at times approximating to scleroderma. There is listlessness and apathy and there may be pathological sleepiness. General muscular weakness is constant and there is marked atony of the gastrointestinal tract with obstinate constipation and a distaste for food. There is commonly a subnormal temperature and complaint of feeling cold. The basal metabolic rate is lowered. All the metabolic processes are retarded and the condition closely approximates to that of hibernation in animals - a condition commonly attributed to some control of the pituitary over the metabolism. Changes in the sexual functions are constant. In the female menstruation ceases and sterility ensues. In the male there is marked weakness amounting to complete impotence; sexual desire is absent in both sexes. Zonderk¹²⁰ points out the disturbance in the salt and water metabolism and considers that the emaciation is due to the inability of the body to retain fluids (Deutsche med. Wchnschr. liv. 1955, 1928).

Hypopituitarism

Underactivity of the pituitary may be a primary condition or it may follow a period of over-activity (as frequently seen in Acromegaly). Depression of the sexual function with loss of desire and impotence and amenorrhoea in the female is characteristic. Primary deficiency commonly results in lack of development and differentiation of the secondary sexual characteristics - the voice remains high pitched in the male and there is an unnatural fulness of the breasts.

Associated with the above are changes in the distribution of the hair and the nature of the skin. In the male the beard and axillary hair are scanty and the pubic hair assumes the feminine type. The body is usually hairless. The skin is smooth in children but becomes dry and atrophic in adults (alabaster skin). There is diminution of sweat.

Adiposity is the rule and a notable feature is the fluctuation in body weight; the fat frequently assumes the typical girdle distribution. Bony development is retarded and dwarfism commonly results.

Mentally there is a backwardness and general cerebral retardation. The basal metabolic rate is depressed and often averages 20-30% below the predicted figure.

The carbo-hydrate tolerance is increased. There is usually polyuria. The pulse may be slow but this

is not constant. There is general fatigability, the blood pressure tends to be low and the temperature subnormal.

Three common clinical types are recognised:

Frolich's syndrome or Dystrophia adiposo-genitalis.

This occurs in children who show complete retardation mentally and physically - they are dull and stupid, show marked hypoplasia of the genitalia and deposits of fat.

The Lorain type.

Mentally these persons are fairly normal and there is no disturbance of their carbohydrate metabolism. There is marked skeletal under-development and the genitalia are hypoplastic.

The Brissaud type.

Similar to the Lorain type but presenting the round, chubby face, general under-development with rudimentary sex organs and deficient body hair. There is a marked tendency to somnolence.

Rowe and Lawrence¹⁰⁵ have recently published a very complete analysis of some four hundred cases of pituitary dysfunction; these were selected from about two thousand cases referred to their hospital for diagnosis.

It is impossible to summarise their findings in full but some of the more interesting points may well be mentioned in this paper.

In their cases it was noted that females predominated in the ratio of 3/2 but no great significance was attached to this in view of other possible causes affecting the proportion.

Biochemically the high incidence of glycosuria was attributed to involvement of the posterior lobe. A striking fact was the frequent finding of a positive result to the para-dimethylamino-benzaldehyde or urobilinogen test of Ehrlich; they consider this test to be of diagnostic value in cases where it is possible to rule out non-endocrine causes. The other urinary findings lead them to think that there is usually a disturbed kidney function associated with pituitary dysfunction - probably due to an indirect metabolic disturbance. There is stated to be a relative and absolute increase in the amount of uric acid eliminated in hypofunctional cases. There is a high residual nitrogen of which one fraction could not be allotted to any known constituent.

The blood chemistry bears out the urinary findings - the high values of the uric acid are striking.

The blood morphology is relatively normal. They did not confirm the findings of others that there is frequently a secondary anaemia nor was there any reduction in the haemoglobin.

There is generally an increase in the lymphocytes (Falts also recorded this finding). The writers con-

sider that lymphoid bloods are commonly found in all endocrine conditions.

Noteworthy is the increase in eosinophils. Nearly one third of their cases showed this finding without any non-endocrine cause being found. The basal metabolic rate was found to follow the functional activity of the anterior lobe. The blood pressure and pulse rate follow a downward trend except in purely hyperfunctional cases.

The profound influence of the pituitary on sugar metabolism is well shown and the galactose tolerance test findings are instructive.

There is much interest in the paper under discussion on such points as age and race incidence; on family and marital history but space forbids their inclusion in this paper.

Of interest is the high incidence of previous tonsilectomies and sore throats.

Of the various signs and symptoms recorded in the series of cases the following are the more important:

Changes in weight (greater than 10%)	73%
Disturbance of menstruation	51%
Asthenia	36%
Headache	34%
Constipation	29%
Hypertrichosis	28%
Low blood pressure	28%
Paraesthesias	20%
Tinnitus	17%
Deafness	15%
Vertigo	14%

Radiological abnormalities occurred in only 11%

of all the cases. The eye findings in eighty four cases were:

Enlarged blind spots	64%
Contracted visual fields	29%
Yellow discs	19%
Hazy discs	10%
Choked discs	3%
Vessels sclerosed	3%
Optic atrophy	1%

The importance and interest of the paper quoted from is that nearly all the cases were not diagnosed by the general practitioner and few of them showed the text-book signs of pituitary dysfunction. The authors stress the point that these less acute departures from the normal are a good deal more common than has been supposed and they are consequently frequently missed.

The diagnosis in the cases recorded was very carefully made after repeated examinations extending over the time of the residence of the patients in hospital; great care was taken to exclude non-endocrine causes.

The common trend in the majority of the cases was towards hypofunction of the anterior lobe with hyperfunction of the posterior lobe.

Therapeutically good results were obtained in many cases; the dosage employed was very considerably larger than that usually given: 1-2- grams being the usual dosage prescribed.

Tumours of the Pituitary

Intra-sellar pituitary tumours are found affecting the chromophobe and chromophil cells. The common tumour is the adenoma (first pointed out by Benda in 1900). These adenomas vary considerably in size and may be very small. A point of special importance is that the effects of the tumour, apart from those due to pressure on surrounding structures, are due to the greatly increased activity of the cells concerned and these may result from lesions which are microscopic in size and may be frequently missed at post-mortem unless the gland is carefully examined by the serial section method.

The clinical results from overgrowth of certain cells is due then, primarily, to the increased secretion of these cells and secondarily to the effects of pressure one on the other secreting cells of the gland and on the surrounding structures.

Briefly adenomas of the eosinophil cells produce acromegalic signs - hyperpituitaryism. Chromophobe adenomas produce symptoms of hypopituitarism (indirectly due to compression of surrounding cells). Basophil adenomas have been shown (Cushing^{21a}) to produce a syndrome formerly ascribed to a cortico-adrenal tumour in which there is plethoric adiposity, genital dystrophy, osteoporosis and vascular hypertension. This is difficult to correlate with the supposed function of the

basophil cells as secreting the sex-maturing hormone. In conclusion it should be noted that there is a well-known relation between the hypophysis and the adrenal (hyperpituitary states producing related hyperfunction of the adrenal cortex) it is not unnatural that cortico-adrenal changes would as frequently occur in basophil as in acromegaly.

4. THE THYROID GLAND variable amount of colloid -

A. Anatomy: histology: physiology. gland

The thyroid gland consists of two lobes lying on either side of the trachea and larynx; these lobes are joined in front by a strip of glandular tissue called the isthmus. The total weight of the gland in the adult averages 30-60 grams but is subject to wide variations within the normal and to certain fluctuations in the same subject, these variations in weight are particularly common in the female as will be shown later.

The thyroid is developed by immediate outgrowth from the entoderm lining the floor of the pharynx, at a level between the first and second branchial pouches.

During intrauterine life the gland is made up of solid masses of cells without any colloid. At birth the gland is made up of typical regular small vesicles, the majority containing some colloid secretion. The gland is active throughout childhood and reaches its maximum activity in adolescence. During periods of great activity the cellular elements predominate and there is a diminution of colloid: the gland at this stage approximates to the clinical picture of Graves disease. In old age there is a reduction in size of the gland and a general appearance of diminution of function; there is an increase in fibrous tissue and marked reduction of the secreting cells. The average adult gland consists of numerous vesicles of varying

size and containing a variable amount of colloid - this colloid represents the secretion of the gland and it is removed from the vesicles either by the blood vessels or by the lymphatics, or both. The cells surrounding the vesicles vary in shape and may be columnar, cubical or flattened. There is no basement membrane. Between the vesicles are layers of connective tissue and scattered in this are small cells.

The blood supply is abundant - the thyroid receives more than five times the amount of blood than the kidneys in proportion to their size. There are nerve fibres from both the vagus and the sympathetic and these apparently go to the secreting cells.

The function of this important gland is generally regarded as primarily one of regulating the metabolic processes of the body and this, in general is undoubtedly true. Of great importance is its regulation of growth and thus it is that the gland shows its maximum activity during adolescence. It seems probable that the gland has an important relation to immunity; like so many of the reported functions of the gland, however, it is difficult to decide how much of the influence is of a direct type or how much is due indirectly to its known stimulus to the whole body metabolism.

It has long been known that there is an intimate relation between the thyroid and the sex glands - the thyroid enlarges during menstruation and during pregnancy

and the vasculatiry is greatly increased at these times. It seems that the gland is of great importance to the female and her sex life. Hammett¹⁰⁶, experimenting in young rats, found that thyroidectomy caused marked loss of development of the ovary and uterus while in males the growth of the testes and epididymis was not greatly retarded. It is significant that disease of the thyroid is much commoner in women than in men.

Crile¹⁰⁷ has put forward the theory that the secretion of the thyroid regulates the electrical conductivity of the nervous system (he holds that the organism is an electro-chemical mechanism) and this certainly explains some of the effects of over secretion of the gland. Undoubtedly the secretion of the thyroid plays an important part in the functioning of the nervous system - this fact is well brought out by the nervous symptoms which invariably accompany states of hypo and hyper function of the gland (vide infra).

The interrelations of the thyroid with the other endocrine glands are very complex and are not yet known with any certainty - there seems to be a close relationship with the pituitary on the one hand and the adrenal cortex on the other. This matter will be referred to later in this paper. Thyroxine and adrenaline both have a direct influence on the sympathetic nervous system (as opposed to the parasympathetic or vagus); both these secretions appear to sensitise this branch

of the involuntary nervous system.

Experiments made some time ago by Herring on cats proved that feeding thyroid to cats increased the adrenalin content of the adrenal glands.

The chemistry of thyroxine was first carefully worked out by Kendall: he was able to give it a chemical formula. Later this was found to be incorrect by Harington who then gave the composition as para-hydroxyl phenyl ether of tyrosin with 4 iodine atoms). He has since succeeded in synthesizing it.

It has been computed that 1 mgm. of thyroxine will increase the metabolism by an amount equivalent to the oxidation of about 250 gms. of glucose and is responsible for the liberation of 100 calories. It has been shown that iodine is a most important constituent of thyroxine; the gland, apparently has the power to fix iodine; this iodine is held in organic combination in the gland as iodo-thyro-globulin. The maximum iodine content of the thyroid gland is stated to be 25 gms.

B. Pathology of the Thyroid

A great deal has been found out in recent years about the physiology and pathology of the thyroid gland; indeed it is from the pathological picture obtained from its disordered action that we have learned most about its action on body metabolism.

So far thyroid deficiency is the only endocrine deficiency disease in which replacement therapy has met with unequivocal success.

Hypothyroid states

Congenital deficiency or underdevelopment of the thyroid occurs occasionally but the factors producing it are unknown. The condition does not manifest itself till the age of six months or so. The signs of this early thyroid deficiency are primarily those of marked retardation in all the spheres of usual development; the child is late in learning to sit up, walk and talk; mental development is almost non-existent and a state of idiocy may result. The skeleton is small and stunted and the secondary sex characteristics do not develop. The skin is thick, the tongue is large and protrudes from the mouth.

Many degrees of thyroid deficiency occur in adults ranging from complete lack, following total thyroidectomy, to minor degrees which do not attract much attention.

Myxoedema commonly occurs in females; the gland is small and there is little colloid in the vesicles; a varying amount of fibrosis is usually present. As is to be expected there is a general depression of all the functions of the body. Mental activity is retarded, there is slowness of cerebration, defective memory and a general lethargy.



The skin becomes coarse and dry; the hair of the head falls out and becomes noticeably absent from the outer thirds of the eyebrows. There is a deposition of myxomatous matter in the subcutaneous tissues; the individual complains of feeling the cold.

The sexual functions are depressed and amenorrhoea commonly develops. The basal metabolism is reduced - often by 25% or more. The heart rate is slowed and the temperature becomes subnormal.

Simple goitre is a condition of enlargement of the thyroid gland with signs of deficiency; there is hypertrophy of the glandular substance and the follicles are increased in size. The condition is apparently due to a lack of iodine, relative or absolute, in the diet. The administration of 1 gr. of iodine daily is sufficient to rectify the abnormal action of the gland.

HYPERTHYROIDISM.

To this condition several names have been given - Graves disease, Basedows disease, Flajanis disease and Parry's disease. Parry, an English doctor, described for the first time the well known triad of signs - goitre, exophthalmos and palpitation of the heart; he also noted the tremor and nervous manifestations so commonly found in the disease.

The condition is generally regarded as an excessive activity of the gland with an over-product of thyroxine. It has been suggested that there may be some change in the secretion (chemical) or that the

process is a toxic one. The actual etiology of the condition is not definitely known but it is possible that an emotional factor may be partly responsible; there is a noticeable hereditary factor and the disease has frequently been observed to follow an infectious illness. The cardinal symptom is increase in the metabolic rate; the energy output may rise to 50% above the average. The work of the heart is increased and the diastolic period of rest is lessened, and the heart tends to dilate and auricular fibrillation may occur.

The blood sugar is raised and glycosuria may occur. The undue sensitization of the sympathetic system gives rise to the dilated pupils, the exophthalmos and the retraction of the upper eyelid.

Tremor, especially a fine tremor of the hands is frequently present. The central nervous system shows hyperexcitability - there is emotional instability, sleeplessness, nervousness and apprehension and in severe cases a state bordering on mania.

There may be a rise in body temperature, the pulse is rapid and there is a reduction of body weight; the skin is often flushed; the blood pressure is variable.

5. PARA-THYROID GLANDS

These small though important glands are normally four in number and lie on the posterior surface of the thyroid gland; two on the upper portion and two on the lower on each side.

They were first discovered and recorded by Sandstroem in 1880 but nothing was known of their internal secretion at this time. Gley was one of the first to study their physiology. It had been noted previously that total thyroidectomy rapidly produced a condition of tetany and it is now established that this is due to removal of the para-thyroid glands.

Extirpation of the para-thyroids produces a marked fall in the blood and tissue calcium. In tetany the blood calcium falls from its very constant value of about 10 ,g,. per 100 cc. to from 8-6 mgm. per 100 c.c. In 1925 J. B. Collip¹²¹ announced the extraction of a para-thyroid hormone which would prevent or control para-thyroid tetany and which regulated the level of blood calcium (J.Biol.Chem. 63, 395, 1925, 439 and 461, 64, 485, and the Para-thyroid glands - Medicine, 5, i, 1926.

This para-thyroid hormone is called parathormone; it is probably ineffective when given orally and is administered subcutaneously or intravenously. It has been found to be effective in infant tetany and in some cases of nephritis with marked oedema.

Hyperparathyroidism occasionally occurs and is due either to over-activity of a normal gland (?) or to an adenomatous condition. The characteristic symptom of this disease is osteitis fibrosa - a condition of rarefaction of the bones due to the production of a negative calcium balance and consequent loss of bone calcium. This lesion responds to the administration of parathormone. The blood in this state is rich in calcium, diminished in inorganic phosphates and shows a secondary anaemia; there is an excessive excretion of calcium and phosphorous.

It has been suggested that paralysis agitans may be due to parathyroid dysfunction but the glands have been found normal in several cases examined. Chvostek considered that myasthenia gravis and tetany were two opposed conditions and that both might be related to the para-thyroids - there has been little to support this theory.

PINEAL

This small organ, about a third of the size of the pituitary, is situated in the roof of the third ventricle lying over the aqueduct of Sylvius. The average weight is given as varying from .15 gm. to .2 gm. Historically this organ has long been studied and there has been much speculation on the nature of its function. Galen in 1562 described it and considered that it was a gland. Descartes in the next century put forward the somewhat startling theory that the pineal was the noblest organ in the body as it was the seat of the soul. Magendie considered that the pineal had a purely mechanical function in that it regulated the flow of the cerebrospinal fluid. At one time it was regarded as a rudimentary sensory organ, in some way connected with the so-called third eye.

Histologically this organ is now considered to be made up of characteristic parenchymatous cells which are neither nervous nor neuroglial in type (Rio Hortega, 1922 and 1928).

The general histological picture is very variable; it alters considerably with age and according to the amount and distribution of the vascular connective tissue system.

Generally there occur, in young subjects, irregular masses of cells surrounded by reticular connective tissue; this connective tissue traverses the whole

gland and frequently appears in curved and branching filaments. The cell nucleii are of two types: pale, with well marked nucleolus and minute chromatin; and dark nucleii with deeper staining chromatin. Throughout the organ run myelinated nerve fibres. Neuroglia cells and fibres are extensively present; these increase as age advances and the secreting cells diminish in number.

The true pineal cells are peculiar in that each cell can be shown to possess a thin process which ends in a club-shaped extremity; these tuberoso endings are frequently applied to capillaries. Scattered throughout the pineal are collections of calcareous matter, the so-called corpora amylacea or brain sand.

Functionally little is definitely known concerning the pineal. The gland is said to function only during childhood and during this time it is considered to have an inhibiting function on development, and in particular on sexual maturity.

Extirpation experiments have been unsatisfactory on account of the difficulty of the operative procedure and the risk of severe haemorrhage. Feeding experiments have also proved unsatisfactory.

Clinically, cases have been observed to show precocious sexual development and abnormal skeletal growth when the pineal has been found to be the seat of a tumour.

PANCREAS ADRENAL GLAND

Islet of Langerhans. These are collections of epithelial cells which are relatively unstained by the ordinary acid and basic dyes after the usual method of fixation. By special staining methods intra-vitam, however, it is possible to stain the granules which are present in the cytoplasm. These granules are of two types: the Alpha or oxyphil and the Beta or basophil. These granules have certain differing chemical reactions: e.g. the Alpha granules are insoluble in alcohol. There is a plentiful supply of sinus-like capillaries to the islet cells; both myelinated and non-myelinated nerve fibres have been shown to ramify over the surface of the cells. The adrenal occurs in nearly all vertebrates. In

Minkowski and Mehring showed that excision of the pancreas caused severe and rapidly fatal diabetes.

It has been shown that the secretion produced by the cells (insulin) has three distinct actions:

- (1) It enables the tissues to burn sugar;
- (2) It enables the liver and muscles to store sugar;
- (3) It inhibits sugar formation from protein in the liver.

In diabetes it is usual to find some pathological changes in the Islet cells; either there is an extensive fibrosis of the pancreas or else there may be an oedematous condition of the cells themselves.

6. THE ADRENAL GLANDS

Anatomy etc.

These glands are two in number and are situated above each kidney. The right is described as triangular and the left as almond-shaped. The combined weight in the adult human is about 10-11 gms. Accessory adrenal tissue is sometimes found and may be cortical or medullary. Cortical tissue occurs retroperitoneally, on the surface of the liver and kidney and in the space between the testes and epididymis in the male and in the broad ligament in the female.

Accessory chromophil matter may be found in the sympathetic ganglia and sometimes in the carotid body.

The adrenal occurs in nearly all vertebrates. In elasmobranch fishes there is an inter-renal body lying between the two kidneys; its structure resembles the human adrenal cortex. In the same fish chromophil tissue (corresponding to the human medulla) is situated along the lateral sympathetic chain.

The adrenal cortex has a mesoblastic origin and develops from the coelomic epithelium (Wolffian duct); it is of great interest to note that the sexual glands develop from the same area and this explains the close relationship which exists between the adrenal cortex and the reproductive organs.

The medullary portion of the gland is ectodermal in origin and develops from a mass of cells lying near

the posterior root ganglia; the sympathetic nervous system develops from the same original cell mass.

At birth the suprarenal glands are as large as the kidneys and almost as large as the adult gland.

Histology.

Cortex. The cells are arranged in three quite distinct zones: the zona glomerulosa or outer layer lies directly below the capsule; it is composed of small round cells with deeply staining nucleii and cytoplasm which stains faintly pink with eosin; there is a marked tendency for the cytoplasm to be vacuolated.

The zona fasciculata or middle layer is made up of long columns of cells whose cytoplasm is usually very vacuolated. These cells are particularly rich in lipoids and this is responsible for the vacuolated appearance. The lipoid content varies considerably and is most marked at puberty. Between the cell columns run wide capillary spaces.

The zona reticularis is the lower layer and is adjacent to the medullary part; here the cells are large, rounded and well-defined. The blood supply is copious and is greater than any other part of the gland. The vessels open out into wide sinus-like spaces between the cells. The reticular zone increases in width and vascularity with maturity and in the adult is the largest part of the cortex. The

medulla is situated in the central part of the gland and increases in size as age advances. It is composed of large angular cells which stain deeply; the nuclei are well marked but are sometimes difficult to see on account of the deeply staining cytoplasm. The medulla is very vascular, the blood vessels opening out into wide sinuses. Elastic tissue fibres are frequently seen and appear to surround the veins. The medulla is particularly susceptible to post-mortem changes and unless the gland is examined in a fresh state the structure may be radically altered.

The whole gland is surrounded by a fibrous tissue capsule which sends fine trabeculae into the substance of the organ; this capsule increases in thickness with advancing years.

The blood supply is derived from the abdominal aorta and the renal and phrenic arteries; there is an extensive capillary anastomosis. The venous return is by a network of small veins which unite to form a central vein; this vein joins the inferior vena cava on the right side and the renal vein on the left side.

The nerve supply is mainly through the splanchnics (sympathetic) and is stimulatory to the medulla cells. The cerebral centre is believed to be in the floor of the fourth ventricle.

Physiology of Adrenal Glands

Cortex

Extirpation experiments have shown conclusively that the adrenal cortex is essential to life while the medulla is not.

Exactly why the cortex is essential to life is not yet definitely known but the recent preparation of a cortical extract (free from adrenaline) which has a profound influence on Addison's disease throws some light on the problem.

The high lipoid content of the cortex suggests that it has an important influence on fat metabolism. Closely related to the presumed action on fat metabolism is the possible action of the cortex on cholesterol metabolism. A diet rich in cholesterol increases the lipoid content of the adrenal cortex. The cortex enlarges during pregnancy, at which time there is a rise in blood cholesterol.

Schafer has suggested that the lipoid formed in the gland may have some influence on the formation of the myelin of the medullated nerve fibres. Undoubtedly the adrenal cortex plays an important part in the development of the nervous system.

The intimate relation of the adrenal cortex to the pituitary has already been noted.

There is clinical evidence that the adrenal plays an important part in the development of the reproductive

organs; this relationship would be expected from the embryological fact of their related development and from the biochemical fact that they are both rich in lipoids. Cortical tumours in children produce precocious sexual development and when occurring in the female, masculinization. (Bulloch and Sequeira¹²²).

It has been shown that tumours of the medulla have no direct effect on the sex organs (Hutchison, R.¹²³).

In Addison's disease it is not uncommon to find amenorrhoea, absence of libido, impotence and some degree of testicular atrophy; these deficiencies respond to the administration of cortical extract..

It is believed that the cortex has a detoxicating function. Myers¹²⁴ found that the toxic action of cobra venom was greatly reduced by mixing it with adrenal cortex but that medulla tissues had not this effect. Lewis¹²⁵ corroborated this and extended the findings to experimental poisoning with veratrin and morphia in animals deprived of the adrenals; he showed that the lethal dose was considerably smaller than in animals with intact adrenal glands.

Reference will be made later to the detoxicating action of cholesterol.

It is probable that the cortex plays some role in metabolism but the exact mode of action still remains obscure.

Medulla

This part of the adrenal gland is intimately connected with the sympathetic nervous system - this is in keeping with its mode of origin.

Oliver and Schafer in 1894 pointed out the effect of extracts of supra-renal medulla in raising blood pressure; this observation was soon verified by others. In 1901 Takamine succeeded in isolating the active principle in a crystalline form and to it he gave the name epinephrin. This substance is dioxyphe-nylethanolmethylamine; it is closely related to tyrosin from which it may be derived. The substance has now been prepared synthetically but the artificial product does not polarize light and is considerably less potent in its action (laevorotary adrenaline being twelve times as strong as the synthetic substance).

With few exceptions adrenaline acts on all sympathetically innervated structures and produces the same effect as stimulation of the sympathetic nerves; a notable exception are the sweat glands. There is little doubt that adrenaline acts peripherally and not on the sympathetic nerve centres. It acts on the isolated heart and intestine and on the denervated limb. It has been shown that adrenaline acts on a junctional substance between the nerve and the organ, this has been called the myo-neural substance.

Adrenaline is rapidly oxidised and the action

resulting from injections is of short duration. It is doubtful if adrenaline given by the mouth is absorbed at all before it has been broken down by the acid of stomach. The concentration of adrenaline in the blood of the resting animal has been estimated at about 1 in 1,000,000,000 (this of course applies to the general circulation under normal conditions). The concentration in the suprarenal vein is commonly much higher.

In states of bodily stress or emotional strain adrenaline is definitely secreted in quantity and reinforces the action of the sympathetic. (Cannon, W. B.¹²⁶) Bodily changes in Fear, Anger, Pain and Rage, D. Appleton Co. 1915)

It has been shown that the following conditions also increase the outpouring of adrenaline into the blood stream: exposure to cold; fall of arterial pressure; asphyxia; anaesthesia; stimulation of different nerves and hypoglycaemia.

In short the adrenal-sympathetic system is the defence mechanism of the higher animals.

B. PATHOLOGY OF THE ADRENAL GLANDS

In 1855 Thomas Addison published his account of what he called "idiopathic anaemia" and from his pathological investigations he was able to show the association of this condition with a destructive lesion of the adrenal glands. Many theories have been advanced to explain the relationship between the pathological findings and the typical clinical signs of the disease. It is now commonly accepted that the symptoms are due to deficiency of the internal secretion of the suprarenal glands. Until recently it was usually thought that the medulla was primarily at fault and that this explained the low blood pressure which was so constantly present; this idea was sustained by the prevalent conception that the two parts of the gland were quite separate in their function.

It seems, in the light of recent advances, that there is a close functional relationship between the medulla and cortex and that it is not a mere coincidence that the two developmentally separate structures have such an intimate anatomical relationship.

The commonest pathological change met with is a tuberculous process involving the greater part of both glands with marked fibro-caseous changes; not infrequently there is a primary tuberculous focus in the lungs. Less frequently there is a simple atrophy of the glands; sometimes the destruction is due to malign-

nant disease. In a small proportion of cases of typical Addison's disease there is no apparent involvement of the glands. In some cases the abdominal sympathetic ganglia are involved in the tubercular process.

The pathology of this disease is complicated by the frequency of accessory adrenal substance which may not be involved in the disease and which may undergo hypertrophy and help to replace the diseased gland (this will depend to a large extent on the rapidity of the disease as compensatory hypertrophy requires time to develop adequately).

Addison's disease, then, in the light of modern pathology, depends on a destructive lesion of both suprarenals; it can be acute or chronic and results in partial or complete suppression of the internal secretions of the gland.

The disease occurs generally in middle age and tends to affect females more than males. It usually develops gradually and the cardinal symptom is progressive asthenia - lack of interest, inertia and marked fatigability.

The blood pressure is markedly lowered and the temperature is subnormal. There is an anaemia and digestive disturbances are common.

Pigmentation is nearly always present (75%). It is most common on the face and neck, the back of the hands and all areas subjected to irritation. The linea

alba are especially prone to develop it.

There have been many explanations to account for this striking deposit of pigment; the most probable one appears to be that it is due to the excessive accumulation of tyrosin in the skin (normally this body is utilised by the adrenal medulla in the manufacture of adrenaline) where it is acted on by a ferment known as tyrosinase with the production of a pigment called melanin which is deposited in the Malpighian layer of the skin.

Until recently the prognosis in Addison's disease had always been grave, and the disease usually proved fatal in a few years at the longest from the date of onset.

The recent work of Swingle and Pfiffner and others referred to previously has opened up a completely new field of investigation and has, it may confidently be expected, produced an important therapeutic agent for this hitherto fatal illness.

Little is known about conditions of hyperfunction of the adrenal glands; prolonged stimulation of the medulla, as occurs in fear and possibly other emotional stresses, may produce a condition of hyperadrenalinaemia and this may conceivably result in a raised blood pressure and general arteriosclerosis; this is, however, a very debateable point and conclusive evidence is lacking.

Tumours of the adrenal cortex and the hypernephromata

are known to be associated with changes in the sexual apparatus - commonly a precocious sexuality and in women a tendency to develop male characteristics. Excessive growth of hair may occur and sometimes obesity is marked.

THE SEX GLANDS

The greater part of the sexual apparatus in both sexes is devoted to reproduction and falls outside the scope of this paper.

Both the testes in the male and the ovaries in the female have important endocrine activities and it is necessary to consider the anatomy and physiology of these components.

In general it may be said that in both sexes the internal secretions of the corresponding gonad are intimately connected with the determination of the secondary sexual characteristics; this influence is beyond dispute at the time of puberty and it seems probable that it is operative in utero and determines the differentiation of the primitive genital tract.

A. MALE

Leydig¹²⁷ appears to have been the first to demonstrate the presence of groups of cells lying in the connective tissue of the testicle and outside the seminal vesicles (Zeitschr.f.wissensch.ii.1850). After this worker these cells have been called the cells of Leydig. Steinach¹²⁸ supplied the name of puberty gland to the same structure (Pflugers Archiv. 144. 1912).

In 1903 Ancel and Bouin¹²⁹ were the first to ascribe an internal secretion to the cells of Leydig and they suggested the name interstitial gland. (Arch.de Zool. experim. 1, 1903 and elsewhere).

The interstitial cells develop from the mesoderm of the germinal ridge: they appear first about the 5th or 6th week when the embryo is about 25mm. long. They increase in number and are at their maximum about the fourth month of intra-uterine life. This period is called the first puberty and marks the time when the asexual embryonic form first becomes differentiated into one or other sex. At birth they are diminished in number and there is a long quiescent period until the onset of puberty proper when they are found to be greatly increased in numbers.

They remain well in evidence during adult life; may show a slight reduction as age advances and finally may increase slightly in old age.

These apparent changes in numbers may be relative to the increase and subsequent decrease in size of the seminal vesicles.

The interstitial tissue varies greatly in amount in different animals. It is well developed in the cat and less so in the dog and mouse. In man it is usually quite well seen and as above stated is present throughout adult life.

It is interesting to note that in cryptorchidism, where the testes have failed to descend into the scrotum, the seminiferous tubules remain infantile in structure while the interstitial cells are often hypertrophied; the individual is sterile if the condition is bilateral

but the secondary sexual characteristics develop normally. The interstitial cells remain intact after ligation of the vas deferens - a proceeding which causes the seminiferous tubules to undergo a degenerative change; this fact was the basis of Steinach's work on rejuvenation (this work does not appear to have had sufficiently accurate corroboration to be scientifically acceptable).

Exposure of the testicle to X-rays in sufficient dosage to destroy the seminiferous tubules does not adversely affect the interstitial cells. In cases in which the seminiferous tubules have been destroyed and the interstitial cells have remained intact the only demonstrable results have been loss of the reproductive function. The secondary sexual attributes remain intact and there is little or no endocrine upset.

As opposed to this are the effects resulting from injury or ablation of the interstitial cells. In practice this can only be done by experimental castration or as a result of complete disorganisation of both testicles - necessarily involving both seminiferous tubules and interstitial cells.

If the testes are removed before puberty the rest of the reproductive system fails to develop and the secondary sexual characteristics do not appear; there is absence of hair on the face; the larynx remains juvenile and the pubic hair is of the female type. There

is a tendency to gigantism (hypertrophy of anterior pituitary) and often a marked deposition of fat; there may be a striking mental depression.

Castration after puberty produces similar changes though of course the skeletal changes do not occur; there is loss of sexual desire at an early date.

The later castration is performed the greater the number of the sexual characters which remain in the castrate (Lipschutz¹³⁰). (The Internal secretion of the Sex glands; 1924, W. Heffer & Sons, Cambridge).

Structure of the Interstitial Cells.

The interstitial cells are polygonal in shape; each possesses a large spherical nucleus and a well marked nucleolus; there may be a double centrosome (Schafer). The cytoplasm of the cell is stained well by eosin while the nucleus has the usual basophil reaction.

The cytoplasm frequently contains inclusions of a fatty nature; opinion on these lipid inclusions is very divided. Mott¹³¹ considered the lipid played a very important role in the production of nucleic acid upon which substance depended the process of spermatogenesis. Diminution of the lipid content occurred in regressive pathological processes. (Mott, Normal and Morbid Conditions of the Testes - B.M.J. Nov.22 and 27 and Dec.6th 1919; also Mott and Miguel Prados y Such. Further Studies

y Such. Further Pthological Studies in Dementia Praecox, especially in relation to the Interstitial cells of Leydig. Proc. Roy.Soc.Med. 1922 xv).

Lipschutz¹³⁰ considers that it is not possible to draw any conclusions as to the function of the cells from the presence of fatty inclusions nor does he think they are a characteristic feature of the interstitial cells. (Lipschutz. The Internal Secretions of the Sex Glands. Heffer, 1924) Various other crystalloid and protein inclusions have been described but little is known about them.

The Golgi apparatus is well marked. It should be noted that the appearance of the interstitial cells is very variable in different species and in the same animal at different periods of growth. They are well developed in the cat and are particularly numerous in the wild boar; in the mouse they are relatively scanty.

The interstitial cells are embedded in connective tissue strands which run between the seminiferous tubules. It is common to find empty spaces between the groups of interstitial cells and nearby tubules - these spaces were thought to be artificially produced during the process of fixation but Wagner has pointed out that granular masses can often be seen in these spaces and that they occur after fixation in many different kinds of fluid; they probably play some part in the function of the gland which is at present obscure.

Interstitial cells can develop from connective tissue cells and transition stages from the spindle-shaped connective tissue cell to the fully formed interstitial cell can be seen.

It seems doubtful if mitotic division occurs; Wagner reports two cases of it but both these were under experimental conditions; Mott thinks that mitosis occurs. Pigmentation occurs in the interstitial cells; this occurs first during late adolescence and increases with advancing age.

Function

That the testicle possesses an internal secretion has been proved beyond all doubt; the experimental results of castration and the natural study of eunuchs; the results of tying the vas deferens and studies in testicular grafts have all demonstrated that the testicle produces a secretion which passes into the blood and modifies the growth of the body and controls the development of the secondary sexual characteristics. It has been assumed that this internal secretion is produced by the interstitial cells but the matter has not been absolutely settled. Lipschutz¹³⁰ is very guarded in accepting the interstitial cells as the sole origin of the internal secretion. Schafer¹³ inclines to the view that the interstitial cells alone produce the active male autacoid; the writer is of the same mind.

opinion. It must be emphasised that in all the experimentally produced conditions in which the seminiferous tubules become atrophied and the interstitial cells frequently show an increase it is the rule to find preservation of the secondary sexual attributes, in fact these may show an apparent hypertrophy (note also the reports of Steinach following ligature of the vas). Of probably even greater value as demonstrating the presence of an internal secretory function of the testicle are the more recent investigations of the effects of tissue extracts. The first of these observations were made by Koch and McGee in 1927¹³³.

Moore, Gallagher and Koch¹³⁴ in 1929 produced further experimental evidence that the injection of testicular extract (intravenously) into brown leghorn capons produced a remarkable growth of comb, wattles and ear lobes; the response was very rapid and the increased growth was noticeable within some three days.

SEX GLANDS

B. Female

The human ovary is composed of a highly vascular stroma consisting of connective tissue which contains many spindle-shaped cells. Embedded in the substance of the stroma are the Graafian follicles; these contain the ova and at a later stage the corpora lutea.

The Graafian follicles are formed by an ingrowing of the epithelium of the germinal ridge. There are two layers of cells surrounding the ova, an inner and outer theca layer; the inner theca is credited with an internal secretion.

At puberty the follicles increase greatly in size and the liquor folliculi is formed; this is also supposed to have an endocrine function.

Ultimately the follicle bursts and liberates the ovum (ovulation); this occurs during the mid-menstrual period.

The extruded ovum passes to the uterus via the Fallopian tube and if it should become fertilised it becomes fixed to the uterine wall. In any case, whether fertilisation occurs or not, the uterine mucosa has by this time undergone changes in preparation for the fertilised ovum; these changes entail a shedding of the epithelium with rupture of the superficial blood vessels (menstruation). If the ovum has

not been fertilised it is also expelled. These changes in the uterus are termed the oestrus cycle.

After the discharge of the ovum from the Graafian follicle the latter undergoes a marked change; the epithelium (membrana granulosa) becomes greatly thickened by increase and enlargement of its cells and there is a deposit of yellowish pigment; this newly formed structure is called the corpus luteum. This mass of cells becomes very vascular and large theca cells appear - these theca cells also become pigmented. If the ovum becomes fertilised and pregnancy is started the corpus luteum undergoes further development and becomes greatly enlarged; it is then known as the corpus luteum of pregnancy. On the other hand if the ovum fails to become fertilised the existing corpus luteum undergoes regressive changes and finally disappears leaving however a scar of fibrous tissue to denote its former presence. Such a corpus luteum is known as a corpus luteum spurium. Throughout the connective tissue there are groups of interstitial cells; these are poorly marked in the human body but are very conspicuous in some animals.

The above is a very brief account of the structure of the ovary and the cycle of changes which takes place therein. An excellent description is given in Marshall's Physiology of Reproduction. It will be seen that the problem of the internal secretion of the ovary is by

no means as simple as that of the testes. There are many possible sources of autocoid secretion and there has been and still is much controversy as to the site of origin of the known internal secretions.

Three hormones having specific action are known to be produced in the female reproductive organs; two are formed in the ovary and one has been isolated from the placenta.

The Graafian follicle has been shown to produce a secretion to which the name Theelin or Oestrin has been given. This was first demonstrated by Allen and Doisy in 1923¹³⁵. The substance was found to be present in the liquor folliculi of the unruptured follicle. Injection of this substance into castrated rodents produced the characteristic changes of oestrus (especially easy to demonstrate by the vaginal smear method introduced by Stockard and Papanicolaou¹³⁶). Later this hormone was prepared in a crystalline form. There is some doubt as to the specificity of this substance as it has been found that this oestrogenic action is given by extracts from many widely differing sources; it can be produced by extracts of urine, faeces and milk as well as amniotic fluid and it is present in some vegetable matter.

The corpus luteum is the origin of the second hormone under consideration; this is called progestin. The action of this substance is on the uterus where it

appears to be responsible for the processes involved in the embedding of the ovum in the uterine mucosa. The work of Frankel, Loeb, Bouin and Ancel has shown that extirpation of the ovaries or injury to the corpus luteum in pregnant animals invariably terminates the pregnancy. These conclusions were verified by Corner and Allen¹³⁷ in 1929. These workers were able to prevent abortion in ovariectomised animals by administration of corpus luteum extract. Progestin apparently has an inhibitory effect of oestrin.

The corpus luteum hormone referred to as progestin has been called the Alpha hormone by Wiesner¹³⁸; oestrin, theelin or folliculin has been called the Beta hormone.

Emmenin is the name given to an extract obtained from the placenta. Wiesner was the first to experiment with placental extracts and his technique was adopted by Collip¹³⁹.

Wiesner obtained an extract which when injected into immature rats (female) produced oestrus and increased growth of the ovary; corpora lutea were, however, present in the ovaries at the time of oestrus.

This same extract injected into male immature rats provoked an increase in size of the prostate and seminal vesicles; it was not a sex-specific hormone.

Collip was able to extract three fractions from the placenta. The second fraction, which was alcohol soluble and was free from oestrin, was called emmenin.

Emmenin has been found to be active when given orally; it is one of the few hormones which, at the present time, is at all certain in its action when given by mouth (thyroid is of course the other good example). Emmenin produces oestrus in immature female rats when given subcutaneously or orally; the effect is produced within a few days. No demonstrable changes are produced in the prostate or seminal vesivles of the male animal. The effective action is not altered by a previous exposure to pepsin or trypsin.

The other extracts removed from the placenta were thought by Collip to be counterparts of the anterior pituitary hormones (A or ovulation - B or luteinizing).

8A INTERRELATION OF THE HYPOPHYSIS AND THE GONADS

As a result of the great amount of work recently done on the secretions of the anterior pituitary lobe and the ovary it has been found that there is such a close relation between these two organs that it becomes necessary to study their secretions in close association with one another rather than as two separate structures.

It is important in this work to proceed very carefully and to separate accurately the few certain facts from the mass of speculation which abounds on this subject.

It has been shown that at one time the anterior pituitary was supposed to be responsible for two distinct sex hormones; one responsible for follicle ripening (Prolan A or as Wiesner called it the Rho¹ factor); the other possessing a luteinizing function (Prolan B or Rho 2).

It now seems that it is very doubtful if these are distinct hormones; impartial experimenters are not convinced that the two can be separated. Be this as it may it is quite clear that the anterior hypophysis secretes a substance which stimulates the ovary, causing ripening of the Graafian follicles followed by rupture and liberation of the ovum; and the ultimate formation of a corpus luteum.

The ripening follicle now produces oestrin which

acts on the uterus producing the changes and phenomena known as oestrus.

The subsequent formation of a corpus luteum produces progestin which results in the pregestational changes in the uterus and along with oestrin causes hypertrophy of the uterine musculature and mucosa.

That the ovary exercises an influence on the anterior lobe of the pituitary is shown from the effects of castration experiments. If both ovaries are removed there is an increase of basophil cells in the anterior lobe and the blood contains large amounts of ovulation-stimulating substance. The appearance of these 'castration' cells can be prevented by the administration of oestrin. It has been supposed that the cyclical changes in the ovary are related to the pituitary in the following manner. Prolan from the anterior lobe of the pituitary acts on the ovary producing oestrin and Progestin; the progestin then reacts on the pituitary and reduces the amount of Prolan, this in its turn causes the corpus luteum to regress and then freed from the restraining action of progestin the pituitary again turns out Prolan. There are many objections to this hypothesis; as Dale¹⁴⁰ points out there is an enormous outpouring of oestrin and Prolan during pregnancy when presumably the corpus luteum is still continuing to secrete Progestin. The same writer (in the same paper) reports that excision or destruction of the corpus

luteum during pregnancy fails to terminate the condition and that lactation has occurred after a normal delivery. Dale also states that Allen and Wiles have removed the anterior lobe of the pituitary in pregnant animals without the development of any dramatic symptoms. The latter experiment is of particular interest as it has been generally accepted that the anterior lobe is essential to the viability of the ovum (Engelbach¹⁴¹).

Further interactions probably occur between the ovarian secretions and the adrenal cortex and the thyroid - both these glandular structures are known to enlarge during pregnancy though the exact role they play is still somewhat obscure.

In the male it has been shown by Zondek and Aschheim that the prolan, as obtained from urine acted as a stimulant to the entire genital apparatus.

Smith¹⁴² showed that ablation of the anterior lobe of the pituitary in rats led to atrophy of the genital system; with loss of libido and cessation of the female sex cycle. Hypophysectomy prior to ovulation resulted in the ovary showing normal primordial follicles, degenerating follicles and complete absence of corpora lutea. In the sexually mature rat it was found that the corpora lutea persisted for many weeks after the operation. Replacement therapy with fresh living hypophyseal transplants produced oestrus in from five to seven days and the ovaries increased in size

and showed many follicles and corpora lutea. Parallel changes occurred in the testes in the male rat.

Further work by Zondek and Ascheim¹⁴³ and Smith and Engle¹⁴⁴ showed that anterior pituitary transplants into immature female rats and mice resulted in precocious sexual maturity with the formation of numerous follicles, super-ovulation, enlargement of the uterus and cornification of the vagina. These results were not produced if ovariectomy had preceded the transplants; the changes were produced after removal of the Thyroid and adrenals. Engle¹⁴⁵ found the ovarian response (follicle formation) to anterior pituitary transplants obtained from gonadectomized animals was greater than transplants from normal animals (after gonadectomy the basophil cells of the pituitary are increased in size and number and show vacuolation). He concludes that there is a storage of the maturity producing substance in the pituitary and that the gonad secretion acts as a release mechanism without whose influence the pituitary will not give up this hormone. It is interesting to note that the male pituitary though smaller than the female is more potent in inducing sexual maturity.

B. INTERRELATION OF THE PITUITARY WITH THE OTHER
ENDOCRINE GLANDS

Thyroid.

Considerable research has been devoted to the relationship between the thyroid and the pituitary; this has been extensively demonstrated in the amphibia. In the case of warm-blooded animals the earlier results were conflicting but there is considerable evidence to show that the anterior lobe of the pituitary stimulates the thyroid; (Benedict, Putnam and Teel¹⁴⁶) showed that the injection of alkaline extracts of anterior pituitary in dogs produced hypertrophy of the thyroid. Enlargement of the thyroid is frequently observed in acromegaly. Crew and Wiesner⁷⁸ consider that this thyroid stimulating function of the anterior pituitary is subserved by a special hormone which is distinct from the growth-promoting and gonad-stimulating hormones.

Smith (P.E.)¹⁴⁷ showed that removal of the pituitary anterior lobe resulted in a decrease in weight of the thyroid and in the production of a flattening of the thyroid epithelium; transplants of anterior pituitary induced reparative changes in the gland. (J.A.M.A. 88, 158, 1927). It would seem from these experiments that the lowered metabolic rate found in cases of pituitary insufficiency is probably due to an indirect thyroid failure due to the lack of the stimulating secretion from the anterior pituitary lobe. The

converse is well seen in the active phase of acromegaly.

Adrenal cortex.

Ascoli and Legnani¹⁴⁸ working with dogs and Smith (ibid) using rats demonstrated that destruction of the hypophysis resulted in atrophy of the adrenal cortex. It was also shown by Evans that the administration of anterior lobe extract to rats led to hypertrophy of the adrenal cortex. It has been noted that the adrenal cortex is frequently large in acromegaly and small in Simmonds disease (pituitary insufficiency). Clinically it is interesting to note the similarity between Addison's disease and pituitary hypofunction; in both conditions there occur the same marked muscular weakness; low blood pressure and gastro-intestinal atony.

ENDOCRINE STUDIES IN MENTAL DISEASE

A. General

Theories of the causation of mental disease are legion and the whole question of the etiological factor in psychiatry has passed through many phases and it is clear that even up to date there is no unanimity of opinion on this controversial subject.

For a long time there has raged the battle of mental versus physical factors as the causative agent and unfortunately this war still continues. There remain the two camps, the psychogenic and the physiogenic, each with its ardent adherents, each opposing the other; each with but little interest and still less reliable knowledge of the other. It is all rather pathetic and a little tragic to witness the almost frenzied opposition between the opposing forces.

Common sense dictates that there must be two sides to the question and accordingly two modes of approach and investigation; this view point is slowly being realised and it is to be hoped that in the near future this basic factor will be universally acknowledged and there will be a spirit of friendly cooperation between all workers; by this means there should be built up a broader conception of the interaction of mind and body.

It will not be out of place at this stage to quote from Engelbach's recent work "Endocrine Medicine"

(Vol. I, p.442-7) on the general incidence of endocrine dysfunction in states of mental and physical disease and deficiency.

President Hoover at the Conference on Child Health and Protection in 1930 gave the following somewhat startling figures for the U.S.A. Of 45 million children ten million or 1 in every 4.5 were defective. Of these 1 million had defective speech; 1 million had weak or damaged hearts; six millions were improperly nourished; 657,000 showed behaviour problems; 450,000 were mentally retarded; 328,000 were tuberculous; 342,000 had impaired hearing; 18,000 were totally deaf; 300,000 were crippled; 50,000 were partially blind; 14,000 were totally blind; 200,000 delinquent. Estimating the endocrinopathies as the cause of 10% of the defectiveness in the groups limited to malnutrition, speech defects, behaviourism, mental retardation and delinquency it is found that about 1 million children are suffering from some degree of endocrine upset.

It has been shown that 27% of children at school entrance are over weight while 15% are under weight; a total of 42% have a deviation from their predicted weight.

When the endocrine defectiveness in the remaining 80 million persons in the U.S.A. is added to the above figure for children it is seen that at least 3 million suffer from some endocrine trouble.

It has been estimated that 10-15 % of mental defectiveness is due to endocrine disorder.

Attention has been drawn to the necessity of including a thorough examination of the endocrine system in all cases of disease especially in children.

B. SCHIZOPHRENIC STATES

Kraepelin¹⁴⁹ appears to have been one of the first psychiatrists to suggest that the etiology of this mental disease might be connected in some way with the abnormal conditions found in the reproductive organs. He is the first to have connected the gross changes often found in the endocrines of dementia praecox patients, especially the sex glands, with their mental state.

Dercum¹⁵⁰ suggests that in dementia praecox there is an imperfect development of the whole endocrine system; in some cases the gonads failure may dominate the picture but he seems to think that the thymus is more often at fault.

Kojima¹⁵¹ in his examination of the endocrines in cases of dementia praecox found that some of the glands were undersized; there were striking changes in the sex glands and that there was a tendency to hypofunction of the thyroid gland in the male with hyper activity in the female.

Frankel¹⁵² noted gonad changes in dementia praecox.

Mott¹⁵³ in three contributions to the British Medical Journal gave a detailed report of the study of the testes, normal and morbid. He reports degenerative changes in the spermatozoa of dementia praecox cases with a reversal of the usual basic staining of

the heads to an affinity for the acid stain; this occurred in nearly all cases of persons dying from chronic disease.

All the testes from cases of dementia praecox showed varying stages of regressive atrophy and none, even the earliest cases showed any signs of previous virility.

A. Pezard¹⁵⁴ puts forward the theory that the testes in schizophrenia develop up to puberty and then cease to mature; this results in the usual appearance of the secondary sexual characteristics (sometimes not fully developed) but deficient functioning in later years.

Matsumoto¹⁵⁵ concluded that atrophy of the gonads is more common in schizophrenic cases than in other individuals; Lewis and Davies¹⁵⁶ found similar conditions.

Morse¹⁵⁷ in a study of 27 cases of dementia praecox could not satisfy herself that there were any gross changes occurring which could be referred to the mental state apart from the terminal physical condition of the subject and there was very little evidence of any primary gonad failure.

Geller¹⁵⁸ assumes that in the female schizophrenic there exists an inferior ovarian function with anatomical and physiological hypogenitalism.

Sippel¹⁵⁹ found hypoplasia and hypofunction in a high percentage of cases of schizophrenia and he tried

the effect of transplantation; three of his subjects improved and one remained stationary.

Gibbs¹⁶⁰ suggests that some disturbance of lipid metabolism occurs in dementia praecox and may involve the adrenal cortex. The blood cholesterol readings were low in his cases; no clinical improvement was noted, however, by feeding on cholesterol and the cholesterol content of the blood was not raised.

McCartney¹⁶¹ found that out of 70 living schizophrenics 60% showed eunuchoid characteristics and only 5.7% appeared to have normal testes. Of 40 living dementia praecox subjects 52.5% had undoubted ovarian disease. Pathological examination of 158 male and 24 female schizophrenics disclosed marked endocrine changes. The changes were constant in the gonads; these were hypoplastic.

N. D. C. Lewis¹⁶² regards the catatonic and hebephrenic forms of dementia praecox to be largely dependent upon the inheritance of constitutional factors; firstly an aplasia of the circulatory system with hyperplasia of the lymphatic system and secondly an inadequate vitality of the tissues which shows itself by regressive changes, atrophies and scleroses in the endocrine glands, especially in the pituitary, thyroid and gonads and by aplasia of the adrenal cortex.

This theory has much in common with that of

Mott¹⁶³ who considered that dementia praecox has a genetic origin showing itself as an inadequacy or lack of essential vitality of the higher neurones (neocortical) and in the gonads (The Genetic Origin of Dementia Praecox; Journal of Mental Science, V, lxviii, No.283, 1922).

In 1923 Mott¹⁶⁴ examined the pituitary gland in 110 cases of which 72 were psychotic subjects. He found changes in the pituitary comparable to those he had found previously in the testes; a deficiency in nuclear chromatin and general regressive changes in nearly all the cases of dementia praecox.

Numerous investigators have shown that in schizophrenic states there are frequently clinical signs of endocrine imbalance. Hoskins, R.G.¹⁶⁵ and Hoskins, R.G., and Sleeper, F.H.¹⁶⁶ studied the metabolism in dementia praecox. They found that 40 out of 80 subjects showed definite or presumptive evidence of endocrine deficiency; some improvement followed gland therapy.

C. MANIC DEPRESSIVE STATES

Kraepelin considered that this type of insanity was commonly associated with some metabolic disturbance; this fact can hardly be denied. The general metabolic level in mania is obviously different from that occurring in melancholia. Kraepelin and many others since have hoped to place the metabolic side as a primary factor but up to date it cannot be said that any satisfactory evidence has been produced in this direction.

Kretschmer¹⁶⁷ has attempted to correlate the mental makeup with certain physical characteristics using an anthropomorphic basis. In this study he has divided mankind into two main groups: Pyknics - these are short, thick-set individuals who have a tendency to mood-swings and who are therefore likely to develop a manic-depressive psychosis if the swing is too pronounced. Schizoids, who have long, thin bodies, smooth skins and who show an introverted mental trend; these persons incline to the schizophrenic form of psychosis.

The pyknics are said to possess a cyclothymic temperament; the schizoids a schizothymic temperament. Kretschmer makes three other subdivisions and describes athletics, dysplastics and asthenics.

Broadly speaking this method of classification is sound but it is obvious that it is much more common to find mixed types. (Kretschmer, E. Physique and Character, 1925).

Following the work of Eppinger and Hess¹⁶⁸ on vagotonia Claude and others studied the somatic changes occurring in the excited and depressed stages; they made considerable use of pharmacodynamic methods. In the manic phase there was considerable hyper-excitability of the vagus; the vagotonia preceded the attack often by several days. The beginning of the depressive stage was characterised by headache, poor appetite, constipation, rapid pulse and often some pupillary inequality. It seems reasonable to assume that these general somatic changes, which so often precede the mental state, are in some way linked up with corresponding changes in the endocrine glands.

Nolan Lewis¹⁶⁹ examined the endocrine glands in a series of cases and found atrophies, hypertrophies and hyperplasias present but no definite series of changes could be related to the prevailing mental state. In the pituitary there was a tendency to local fibrosis and hypertrophy of individual cell groups amounting in some cases to adenomatous formations.

The thyroids showed fibrosis and the scars of previous infections. The adrenals showed cortical hyperplasias but not to the same extent as is often found in the paranoid states. The gonads were generally well preserved.

Lewis summarises by assuming that there is frequently evidence of some pathological involvement of

the extra-neural systems, particularly the circulatory and endocrine. He also notes the fact that manic-depressive subjects are especially prone to skin infections.

Walter Freeman¹⁷⁰ has studied the organic constitution in manic-depressive types and gives some interesting figures relating to the size and weight of the endocrine and other organs.

The heart and liver are larger in cyclothymics than in schizothymics. The testes are larger but the ovaries are slightly smaller.

Apart from the testes being larger the male endocrines show little difference in size and weight in the two types. In the female, however, almost all the glands are larger in cyclothymics; this is especially noticeable in the pituitary. Eosinophil cells are fewer in the cyclothymic. The thyroid is considerably larger but the parathyroid difference is less striking. The adrenals are larger in the female cyclothymic. The writer goes on to speculate on these findings coupled with the general appearance of the cyclothymic and considers that these individuals have a stronger biological drive.

Richter, C.P.¹⁷¹ advances the theory of total activity in relation to the manic-depressive states. It is shown that when rats are kept in special cages so constructed that even the slightest movements can

be recorded and when all external stimuli are removed there can be demonstrated a certain rhythm in its periods of movement; space does not permit of anything like a detailed account of these interesting experiments. It was shown that in the female the peak of activity coincided with ovulation; removal of the ovaries caused a decrease of 95% of the original activity. (Slonaker, J.R. Amer.Jour.Physiol.xlviii, 294, 1924.)

A corresponding decrease is noted in the male after removal of the testes. It was also found that removal of the adrenals and pituitary resulted in a decrease of activity. A rather surprising fact is that removal of the thyroid had little or no effect on the total activity.

These interesting experiments are in no way conclusive; they are instructive and stimulating and it would seem that this is a likely field for further research.

Sonden¹⁷² considers that the manic-depressive psychoses are due to some disorder in the nervous system and in the endocrine glands; he is opposed to the toxic origin of this psychosis.

D. ENDOCRINES IN EPILEPSY

Repeated attempts have been made to formulate an endocrine causation for the fits of epilepsy. It has been pointed out that epileptiform convulsions may occur in association with exophthalmic goitre (Falta¹⁷³), and in hypoparathyroid states (tetany).

Schafer¹⁷⁴ and others have noted the tendency of epilepsy occurring in hypopituitary states; tumours of the pituitary are not infrequently accompanied by convulsions.

Tucker, B.R.¹⁷⁵ in a series of 200 radiological examinations of the head found evidence (?) of pituitary disturbance in 31.5%. He concludes from his studies that undersecretion of the pituitary is definitely related to convulsive attacks and that there is often marked benefit from pituitary feeding.

Vizioli, F.¹⁷⁵ notes the association of epilepsy with acromegaly. The same worker examined the ovaries of 17 young epileptic women and found very few Graafian follicles and few scars of old follicles; the general picture was that of an ovary of a post-menopausal woman.

Attention is drawn to some alteration in the composition and staining reaction of the thyroid secretion.

Ely, F.A.¹⁷⁶ found that a migrainous ancestral trend predisposes to epilepsy in the offspring.

Johnston, G.C.¹⁷⁷ states that there are often

changes in the pituitary in epilepsy without gross signs of glandular failure; he advises radiological examination in all cases.

Lennox, W.G. and Cobb, S.¹⁷⁸ quoting Munson and Shaw state that these workers found no constant changes in the pituitary. Of 100 pituitaries examined they found the average weight to be 544mgm., which is 10% less than the normal.

Lennox and Cobb go on to say that only a few cases of epilepsy show clear-cut evidence of pituitary gland disturbance antedating the onset of convulsions; in such patients seizures seem to bear a close relationship to disturbance of the gland.

The evidence of the correlation of tetany and epilepsy in the same patient is very meagre although there would appear to be a field for research in the underlying conditions of both these states. It may be said that similar agencies will produce the respective convulsions in those predisposed to the special condition.

There seems little evidence that the adrenals can be implicated in the causation of the epileptic fit. Vollard¹⁷⁹ in 40 autopsies found abnormality in only one case (tuberculosis).

There seems to be no conclusive evidence that the thyroid is directly concerned or at fault in epilepsy; various reports on the effects of the administration of thyroid are found in the literature; in some cases

there is reported benefit, in others the condition has been made worse. Autopsy reports are equally uninformative.

Occasionally it has been found that epileptics have persistent and enlarged thymus glands but there does not seem to be any direct connection between this and the fits and the results of feeding experiments are unsatisfactory.

The sex glands have in their turn been examined and to some extent blamed but here again there is no conclusive evidence. It is common knowledge that female epileptics have menstrual disturbances but as these are common to so many mental conditions it is unwise to try and deduce too much from this fact.

It will be seen from the above brief review of the literature on the subject that while there is some evidence of endocrine participation in the epileptic syndrome there is a vast amount of work to be done before any glandular pathology can be substantiated. It would seem that the pituitary gland is the one to which prime importance should be given; its secretions are carried first to the brain from both lobes and little or nothing is known of a possible action of the various secretions on the central nervous system; indeed the recent brilliant researches of Cushing only tend to complicate the picture and to show us how little we really know of the interaction of this gland and the important vegetative centres in the hypothalamus.

Gland weights recorded in grams.

Body weights recorded in stones and lbs.

Body heights recorded in feet and inches.

Body weights recorded in stones and lbs.

Body weights recorded in stones and lbs.

Body heights recorded in feet and inches.

Gland and Organ Weights in Epilepsy

Sex.	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M
Age.	31		31	17	29	47	20	50	47	23	43									
Height.	5' 4"		--	5' 11"	5' 8"	5' 4"	5' 2"	5' 10"	5' 9"	5' 6"	5' 7"									
Weight.	6-11		7-0	6-13	9-5	7-4	6-1	9-8	9-4	9-0	6-10									
Brain.	1370		1150	1520	1400	1240	1150	1010	1470	1430	1040									
Liver.	1050		1150	1130	1390	900	1250	1610	1300	1490	1020									
Spleen.	100		100	120	135	100	265	190	90	130	120									
Pituitary	.9		.69	.5	.9	.4	.55	.65	.45	.65	.45									
Thyroid.	10		19	14	37	19	18	22	23	14	23									
Pineal.	.1		.51	--	.4	--	.15	.2	--	--	.15									
Adrenals.	12		17.5	10	14	11	10	10	10	18	8									
Gonads.	5		--	21	28	5	25	39	25	30	21									
Cause of Death	Status Epilepticus		Pulm. T.B.	Epilepsy.	Status Epilepticus	Status Epilepticus	Broncho-pneumonia	Status Epilepticus	Status Epilepticus	Status Epilepticus	Pulm. T.B.									

Gland and Organ Weights in Epilepsy

Sex.	F	M	F	M	F	F	F	
Age.	31	19	42	24	18	68	18	
Height.	5' 6"	5' 7"	--	--	5' 2"	5' 3"	4' 9"	
Weight.	6-5	10-0	8-5	8-12	4-11	6-4	5-6	
Brain.	1210	1390	1350	1260	1190	1200	740	
Liver.	1650	1490	1490	1400	870	1220	870	
Spleen.	290	230	220	100	30	130	80	
Pituitary..	.75	.5	.7	.65	.5	.9	.5	
Thyroid.	25	20	23	25.8	25	55	18	
Pineal.	--	--	.25	--	--	--	.1	
Adrenals.	9	10	10	9	13	17	16	
Gonads. 1 ovary		45	14	37	5	6	3	
Cause of Death	Acute Infective Endocarditis	Status Epilepticus	Lobar pneumonia	Status Epilepticus	Broncho-pneumonia	Broncho-pneumonia	Acute bronchitis	

Gland and Organ Weights in Schizophrenia

Sex.	F	F	F	F	F	M	M	M	M	M	F
Age.	23	34	33	37	45	23	25	26	42	34	
Height.	5' 1"	5' 8"	5' 1"	--	5' 6"	5' 8"	5' 8"	5' 9"	5' 7"	5' 2"	
Weight.	4-4	6-11	5-12	5-6	7-6	7-4	9-1	6-11	7-5	6-2	
Brain.	1150	1090	1100	1240	1320	1390	1390	1370	1390	1170	
Liver.	1000	1340	1650	1400	2120	1200	1350	1320	1370	1140	
Spleen.	90	170	170	160	200	130	170	160	100	90	
Pituitary.	.6	.6	.65	.85	.85	.7	.7	.45	.6	.7	
Pineal.	--	--	--	.2	.2	--	--	.35	--	--	
Adrenals.	10	13	12	22	16	10	10	11	12	12	
Gonads.	7	8	10	6.5	5	30	24	23	14	6.5	
Thyroid	10	17	13	27	17	20	41	13	12	14	
Cause of Death	Pulm. T.B.	Mytrial Stenosis	Pulm. T.B.	Broncho-pneumonia	Lobar-pneumonia	Acute Bronchitis	Acute Delirious Mania (?)	Pulm. T.B.	Pulm. T.B.	Pulm. T.B.	

Gland and Organ Weights in Schizophrenia

Sex.	F	F	M	F	F	M	F	M	F
Age.	45	36	20	41	39	30	34		
Height.	5' 0"	5' 3"	6' 1"	5' 1"	5' 5"	5' 7"	5' 1"		
Weight.	7-1	7-7	10-2	--	10-11	6-8	6-4		
Brain.	1270	1370	1450	1100	1350	1470	1180		
Liver.	1200	1830	1690	1300	1750	1270	1640		
Spleen.	130	180	120	120	170	80	130		
Pituitary	.8	.65	.6	1	.85	.9	.65		
Thyroid.	15	25	27	26.7	23	11	29		
Pineal.	--	.1	.17	.1	.45	.45	.2		
Adrenals.	19	18	12.7	15	15	10	18		
Gonads.	5	13	18	11.8	10	32	5		

Cause of
Death

Empyema
Thoracis

Pulm. and
Intestinal
T. B.

Acute
Bronchitis

Influenzal
Broncho-
pneumonia

Ischio-rectal
Abscess

Acute
Bronchitis

Mitral
Disease

Gland and Organ Weights in Manic-Depressive States

Depressive States.

Cause of Death	Pertinephric Abscess: myocardial degeneration.	Acute Endocarditis	Pulm. T.B.	Mitral Disease	Acute Bronchitis	Carcinoma (Gastric)	Broncho-pneumonia	Cerebral Haemorrhage	Chronic Intestinal Nephritis	Pulm. & Intestinal T. B.
Sex.	M	F	F	F	M	F	F	F	F	F
Age.	72	51	39	65	76	57	49	67	54	55
Height.	5' 3"	5' 5"	5' 2"	4' 1"	5' 6"	4' 9"	5' 7"	5' 3"	5' 4"	5' 5"
Weight.	6-8	7-2	5-0	4-8	7-8	4-6	5-7	9-2	6-3	5-7
Brain.	1420	1330	1170	1370	1420	1040	1390	1140	1220	1290
Liver.	1070	1170	1420	940	1440	700	920	1060	1100	1230
Spleen.	170	250	200	90	120	80	100	140	210	110
Pituitary	.65	.9	1.3	.8	.6	.5	.5	.6	.9	.7
Thyroid	21	31	30	31	32	13	94	25	11	17
Pineal	--	--	--	--	--	.15	--	.2	--	.15
Adrenals	--	10	11	10.5	15	9	11	5.2	10	12
Gonads.	--	3.5	12	3.3	32	3.5	3.7	3	2	5

Gland and Organ Weights in Manic-Depressive States

Depressive States

Sex.	F	F	M	F	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M
Age.	28	33	48	49	52	57	63	50	36	39										
Height.	5' 9"	5' 5"	5' 9"	5' 5"	4' 11"	5' 4"	5' 6"	5' 3"	5' 7"	5' 1"										
Weight.	5-10	5-10	8-12	7-0	4-7	7-9	6-13	5-9	6-13	4-13										
Brain.	1190	1270	1230	1460	1050	1300	1650	1360	1550	1180										
Liver.	3310	1260	2010	1150	1040	1350	1500	1770	1000	1000										
Spleen.	190	130	150	80	50	140	140	170	70	70										
Pituitary	.8	.9	.95	.8	.75	.85	.6	.55	.7	.65										
Thyroid.	18	18	23	13	--	23	20	17	30	28										
Pineal.	--	--	.25	.25	--	--	--	--	--	--										
Adrenals.	11	13	10	10	--	9	13	10.6	11	11										
Gonads.	10	14	30	5	--	9	25	6	26	4										
Cause of Death	Pulm. T.B.	Pulm. T.B.	Lobar-pneumonia	Acute Infective Endocarditis	Lobar-pneumonia	Mitral Disease	Myocardial Degeneration Arterio Sclerosis	Pulm. T.B.	Pulm. T.B.	Acute Bronchitis										

Gland and Organ Weights in Psychoses

G.P.I.

Sex.	M	M	M	M	F	F	M	M	F
Age.	60	58	51	36	46	39	46	39	35
Height.	5' 0"	5' 1"	5' 8"	5' 7"	5' 9"	5' 0"	5' 5"	5' 6"	5' 4"
Weight.	7-10	5-5	9-3	7-0	11-0	7-0	13-0	5-10	5-1
Brain.	1425	1040	1370	1190	1410	--	1270	1290	1080
Liver.	1051	890	1470	1550	1350	--	1330	880	1070
Spleen.	110	70	70	80	140	--	140	60	50
Pituitary.	.6	.25	.8	.8	.65	.25	.95	.5	.85
Thyroid.	14	13	14	16	16	22	20	10	23
Pineal.	.05	--	--	--	--	--	--	--	--
Adrenals.	15	12	10	17	14	12	13	7	21
Gonads.	21	22	40	8	32	2.5	5.4	28	5

Gland and organ weights are in gms. Body weights in stones, etc. The body weights are those just preceeding death.

The cause of death in all the above cases was G.P.I. with a terminal pneumonia or bronchitis in most cases.

Manic States

Sex.	F	F	F	M	M
Age.	46	42	50	62	34
Height.	5' 5"	5' 6"	5' 3"	5' 2"	5' 7"
Weight.	5-2	10-9	6-0	7-0	6-12
Brain.	1340	1200	1300	1290	1270
Liver.	1330	1640	875	1450	1370
Spleen.	120	70	95	110	100
Pituitary.	.55	.75	.75	.55	.6
Thyroid.	21	15	17	23	13
Pineal.	.25	--	--	.35	--
Adrenals.	12	12	19	9	12
Gonads.	2.2	9	6	23	24
Cause of Death	Pulm. T.B.	Lobar Pneumonia	Pulm. T.B.	Coronary Thrombosis	Pulm. T.B. Arteric Disease.

Case No. 10. Female, aged 30. Married

Cause of Death --- Pulmonary Tuberculosis.

Mental State

Depressed and miserable on admission. She had some ideas of persecution and thought that her food was poisoned and was poisoned at times and showed mild agitation. She was only four days in hospital before she died.

MANIC DEPRESSIVE CASES

CASE PROTOCOLS AND PATHOLOGICAL FINDINGS

Cases of Depression

As she was refusing food she had to be tube fed. There was cough and irregular pulse and marked wasting. She became progressively weaker and died four days after admission.

Post-mortem

Extensive pulmonary T.B. There was moderate myocardial degeneration but no valvular lesions. The brain showed no gross departure from the normal.

Brain wt.	1360gms.	Folr wt.	52.0gms.
Liver wt.	1770gms.	St.	51.0gms.
Spleen wt.	170gms.	Arm length	20 ins.
Pituitary wt.	.55gms.	Leg "	30 "
Thyroid wt.	17gms.	Skull wt.	450gms.
Adrenals wt.	10.4gms.	Capacity	750ccs.
Ovaries wt.	6gms.	Circum.	211ms.
		Aorta circum.	6cms.
		(Slight atropia)	

Pituitary

In the anterior lobe the basophils predominated; chromophobes were next in frequency while the acid-

CASE NO. D 102. FEMALE, AGED 50. MARRIED

Cause of Death --- Pulmonary Tuberculosis.

Mental State

Depressed and miserable on admission. She had some ideas of persecution and thought that her food was poisoned. She was restless at times and showed mild agitation. She was only four days in hospital before she died.

Physical State

She was in a very weak state on admission and had signs of active and extensive tuberculosis in both lungs. As she was refusing food she had to be tube fed. There was cough and irregular pyrexia and marked wasting. She became progressively weaker and died four days after admission.

Post-mortem

Extensive pulmonary T.B. There was considerable myocardial degeneration but no valvular lesion. The brain showed no gross departure from the average.

Brain wt.	1360gms.	Body wt.	5st.9lbs.
Liver wt.	1770gms.	" ht.	5ft.3½ins.
Spleen wt.	170gms.	Arm length	20 ins.
Pituitary wt.	.55gms.	Leg "	30 "
Thyroid wt.	17gms.	Skull wt.	450gms.
Adrenals wt.	10.6gms.	" capacity	750ccs.
Ovaries wt.	6gms.	" circum.	21ins.
		Aorta circum.	60mm.
		(Slight atheroma)	

Pituitary

In the anterior lobe the basophils predominated; chromophobes were next in frequency while the eosino-

phils were markedly reduced. The basophils stained well and had small dark nucleii with good chromatin. The eosinophils were scanty and the cytoplasm was granular and vacuolated; the nucleii were irregular and seemed to be flattened. The chromophobes were numerous and the nucleii showed good chromatin. The vascularity was diminished and there was some increase of fibrous tissue. The cleft was obliterated and no posterior lobe was seen in the section.

Thyroid.

Appeared pale and homogeneous. Not sectioned.

Adrenals.

Of average size and appearance but rather thin and flattened. The cytoplasm stained faintly pink and showed marked vacuolation and thinning out. The nucleii stained well and looked healthy though some were very deficient in chromatin. The medulla was undergoing degenerative changes (P.M.).

Ovaries

The stroma was highly cellular, both the connective tissue and the epithelial cells staining well. Several old luteal scars were seen but no recent luteal tissue. No Graafian follicles. The blood vessels were markedly thickened.

CASE NO. D. 57. FEMALE, AGE 49 YEARS. SINGLE. HOUSE-
WIFE.

Cause of Death --- Acute Infective Endocarditis

Mental State

On admission was depressed and agitated. She had marked ideas of her own unworthiness and of her own failure in life. She was a potential suicide and was placed on special precaution. She was continually picking herself and was never at rest.

Physical State

Patient was admitted with a fracture of the elbow caused by jumping out of a window with presumably suicidal intention. The heart was enlarged and the bloodvessels arterio-sclerotic. For a few days before death she ran a slight temperature. She died within a fortnight of being admitted.

Post-mortem

showed marked injection of the endocardium and aorta but apart from this the organs appeared fairly healthy.

Body wt.	7st.	Body ht.	5ft.5ins.
Brain "	1460gms.	Arm length	20ins.
Liver "	1150 "	Leg "	35ins.
Spleen wt.	80 "	Skull wt.	540gms.
Pituitary "	.8 "	" capacity	950ccs.
Thyroid "	13 "	" circum	21½ins.
Pineal "	.25 "	Aorta	51mms.
Adrenals "	10 "	(Infected: Slight atheroma)	
Ovaries "	5 "		

Pituitary

Appeared large, with a relative increase of the

posterior lobe which was rather friable. In the anterior lobe there was some general breaking up of the cytoplasm with considerable vacuolation. The chromophobe cells predominated; the nucleii of these cells, as was the case with the other types, appeared to be less well stained than usual and the chromatin was deficient. The basophil cells were prominent and were nearly as numerous as the chromophobes. The eosinophils were numerous but were not well stained and the nucleii were pale. The vascularity was average but there was a marked increase of fibrous tissue. The cleft was well marked and wide but was devoid of colloid. The pars intermedia was well marked and showed acinar formation of eosinophil cells with a good many chromophobes; there was considerable invasion of the posterior lobe with cells. The posterior lobe was very cellular; there were some eosinophil granules; the vascularity was above the average and there was no pigment.

Thyroid.

Small, symmetrical and homogeneous. Not sectioned.

Adrenals

Asymmetrical. Generally the cytoplasm was broken up and there was considerable vacuolation. The nucleii in the zona glomerulosa and fasciculata were rather indistinct but stained fairly well; in the zona reticularis they were much better demarcated. The medulla was wasted and contained many cavities (probable P.M.

change). There was some amorphous blueish substance in these cavities.

Pineal

Rather large and friable. Much pink granular cytoplasm was present and the nuclei lying in this were of the chromophobe type (pituitary). The vascularity was above the average for this gland.

Ovaries

These were small and fibrous and showed no gross abnormality.

CASE NO.D.168. MALE. AGE 49. VOLUNTARY PATIENT.
OCCUPATION - SHOP ASSISTANT. SINGLE.
2nd ATTACK

Cause of death --- Asphyxia by hanging.

Mental State.

On admission was depressed, retarded and dull. He admitted that he could not control himself and wanted to be in hospital where he could be controlled. He had impulses to injure those he loved but there was often amnesia for these ideas after their occurrence. There was a history of hearing imaginary voices extending over a fairly long period prior to admission. There were hypochondriacal ideas of obstruction of the bowels and that his stomach was dead.

Physical State

On admission there were no signs of any organic disease. The Wassermann reaction was negative; the urinary findings of no importance. All the teeth had been removed and there were upper and lower dentures. The face was long and thin; the eyes blue; the forehead sloped backwards; the pulse was 68 and there was slight tremor of the hands. Three months after admission patient was found hanging in his bedroom at 1 a.m. (he was alive at midnight).

Post-mortem.

Myocardium rather fatty; no valvular lesion. Lungs were congested; no Tardieu spots. Small intestine congested. Brain showed nothing abnormal.

Brain wt.	1350gms.	Body wt.	8st.
Liver "	1320 "	" ht.	5ft.5½ins.
Spleen "	160 "	Arm length	20½ins.
Pituitary wt.	.5 "	Leg "	35 "
Thyroid "	27 "	Trunk "	25½ "
Adrenals "	10.8 "	Skull wt.	420gms.
Testes "	28 "	" capacity	870ccs.
Heart "	240 "	" circum.	22ins.
		Aorta "	48mm.
(Slight, fine atheroma)			

Pituitary

In the anterior lobe the basophils predominated. The eosinophils and chromophobes were numerous. The basophils were not deeply stained and the cells had a diffuse appearance. The nucleii were not deeply stained but the chromatin was fairly well marked. The eosinophils were scattered throughout the lobe; their cytoplasm was granular and took the stain well; the nucleii were large and pale and had little chromatin. The vascularity was increased and there was an increase of fibrous tissue. The cleft was obliterated but there were collections of eosinophil colloid apparently derived from the pars intermedia. The pars intermedia was very irregular being broken up with fibrous tissue. All cell types were represented and were stained quite well. The posterior lobe, which was of average size, was very dense; several hyaline masses were seen and there was a great excess of pigment.

Pineal

The groundwork of this body was of an open fibrillated structure and stained faintly pink; there were several blue staining nucleii which showed good chromatin.

There was no colloid nor calcareous masses.

Thyroid

Average size, appearance and colour. On section there was seen to be a considerable increase of fibrous tissue and the section examined appeared to be completely disorganised. The vesicles were very irregular in size and shape and were filled with pale colloid. The lining cells were flattened and poorly stained and no nuclear structure was seen.

Adrenals

Average size and appearance. The zona glomerulosa and fasciculata were stained faintly with the basic dye; the cytoplasm was extremely vacuolated and the nucleii were very pale and deficient in chromatin. The Zona reticularis stained pink, with some basophil areas; there was no vacuolation of the cytoplasm. The nucleii were more regular in shape and stained fairly well. The medulla stained well and was quite well preserved.

Pancreas

There was marked fibrosis through the section. The ordinary glandular structure showed loss of the typical acinar arrangement and the cytoplasm stained basophil; the nucleii varied in size but were moderately well stained. The Islets of Langerhaus were very broken up but retained their usual staining reactions.

Testes

Slightly below average size and softer than normal. The seminiferous tubules were well formed and the cells had stained well, the nuclei being deeply stained. The spermatocytes showed active mitotic division and there was abundant evidence of spermatogenesis. There was some increase of inter-tubular connective tissue. The interstitial cells were reduced in number and stained poorly; the chromatin was feebly stained and appeared deficient.

Hair distribution

Large amount on trunk, arms and legs. Face and pubes normal.

CASE NO. C 185. FEMALE. AGED 59. MARRIED (5 CHILDREN)

OCC. SPIRITUALIST AND SPIRITUAL HEALER

Cause of Death --- Cerebral haemorrhage.

Mental State

On admission was silent and depressed. She was resistive and faulty in habits, and did not take her food at all well. She was restless and inclined to wander about. There was little or no improvement in her condition during her short time in hospital.

Physical State

There were no signs of organic disease on admission. After three months she had a seizure and died.

Post-mortem

showed a moderate sized haemorrhage into the left internal capsule and lenticular nucleus. The heart showed brown atrophy and fatty change. Aorta showed slight atheroma.

Brain	wt.	1320gms.	Body wt.	9st. 91 lbs.
Liver	"	1320 "		(average 10st.)
Spleen	"	90 "	Arm length	20ins.
Pituitary	wt.	.9 "	Leg	31½ins.
Thyroid	"	10 "		
Adrenals	"	10 "		
Pineal	"	.15 "		
Ovaries	"	3.3 "		

Pituitary

Rather larger than normal. In the anterior lobe the three cell types appeared in about equal numbers. The eosinophils were well stained and granular and showed some vacuolation; the nucleii were pale and lacked chromatin. The basophils were numerous and well

stained; there was a tendency to adopt an acinar arrangement; the nucleii were deeply stained. The chromophobes seemed to be less numerous than usual; their nucleii, however, were well stained. Throughout the anterior lobe the vascularity was increased and there was an increase of fibrous tissue. The cleft was patent but contained no colloid. The pars intermedia was extensive and entirely eosinophil. The posterior lobe appeared normal.

Pineal

This body had the usual appearance but was more active looking than one would have expected for patient's age. There was much pink cytoplasm arranged in a syncytial manner and containing well stained nucleii; in some cases the nucleii were large and pale; both types showed fairly rich chromatin.

Thyroid

The gland was smaller than usual. The general appearance was average. On section the vesicles were seen to contain pink and blue colloid but were not distended with it. The cells varied greatly as did their nucleii; some were well stained and the nucleii were dark; others were very pale with mere shadows of nucleii. There was a general increase of fibrous tissue and the vascularity was increased.

Adrenals

Of average size and appearance. The medulla

was deficient. The zona glomerulosa was very empty looking; the cytoplasm showing extreme vacuolation and being faintly stained (pink); the nucleii were very pale and deficient in chromatin. In the zona fasciculata and reticularis the cytoplasm was more distinct but the nucleii were pale and poor in chromatin. Medulla deficient and wasted.

Ovaries

Small and fibrous. Throughout the section examined there were no Graafian follicles seen; the germinal layer was scanty. There were many scars of former corpora lutea but no recent luteal tissue was seen. The blood vessels showed marked thickening of their walls.

CASE NO. C 24. MALE AGED 40. OCC. JOINER AND BUILDER

Cause of Death --- Lobar Pneumonia

Mental State

Depressed and miserable. Delusions of his own wickedness. No mental change during time in hospital.

Physical State

On admission there were no signs of organic disease. A few months after admission he developed a bilateral pneumonia and died.

Post-mortem

showed extensive consolidation of both lungs; nothing else of importance was noted.

Pituitary

Wt. 55gm. Average size and appearance. In the anterior lobe there was a very marked increase of fibrous tissue; the vascularity appeared about average. The basophils predominated; their cytoplasm was well stained and vacuolated; the cells tended to be smaller than usual and rather angular; the nucleii were deeply stained and the chromatin plentiful. The eosinophils were numerous, well stained and granular; their nucleii showed good chromatin and prominent nucleoli. Chromophobes were reduced. The cleft was irregular and contained a good deal of basophil colloid. The pars intermedia was extensive; there were many acini composed of chromophobe cells and in addition there were many eosinophil cells with small dark nucleii. The

posterior lobe was of customary appearance; the vascularity seemed to be slightly increased. There were a few deposits of pigment and the usual pink hyaline masses.

CASE NO. B 162. MALE. AGED 69. MARRIED (NO CHILDREN)
OCC. LADIES' TAILOR. 1st ATTACK.

Mental State

On admission he was noisy and talkative and in a state of mild mania; he remained in this state during his time in hospital. There were fleeting ideas of persecution; at times he was hypochondriacal and emotional; he was always decorating himself. For short periods he was mildly depressed.

Physical State

On admission there was some arterio-sclerosis and slight cardiac enlargement. There was slight motor impairment and the speech was slow and tended to be slurred. The abdominal reflex was absent. The knee jerks were present and pupils reacted and were equal. Two years after admission he developed pneumonia and died.

Post-mortem

revealed nothing of special interest.

Body	wt.	8st. 4 lbs.
Brain	"	1440gms.
Liver	"	1560 "

Pituitary

Wt. 8gms. In the anterior lobe there was a diffuse increase of fibrous tissue; the vascularity was increased. The most remarkable feature of this gland was the excessive amount of basophil collaoid throughout the anterior lobe; this was contained mostly in acini

lined by eosinophil cells. The eosinophils and chromophobes predominated over the basophils. The staining reactions of the cells was normal and the nuclear chromatin up to standard. The pars intermedia was poorly developed and the cells were scanty and poorly stained. The posterior lobe appeared normal.

Adrenals

The cortical cytoplasm was pale and finely vacuolated; the nucleii were faintly stained; the nucleii of the cells of the zona reticularis were more deeply stained and their chromatin was dark and well shown. The medulla appeared deficient. There was an increase of fibrous tissue throughout the gland.

Testes

These were undescended and small. Unfortunately they were thrown away and no sections were prepared.

CASE NO.C 198. FEMALE. AGED 54. MARRIED

Cause of Death --- Acute Bronchitis.

Mental State

On admission she was depressed and miserable, would not speak and was generally resistive. She later expressed the delusion that her bowels were stopped. She was difficult with her food. There was little or no improvement in her mental state during the ten years she was in hospital before her death.

Physical State

There was nothing special to note about her general physical state either on admission or subsequently. Nine years after admission she died from an attack of acute bronchitis.

Post-mortem

showed muco-pus in the bronchial tubes and general congestion of both lungs. The kidneys were small and the cortex was adherent. The brain showed no gross departure from the average. Aorta showed extensive athroma.

Brain	wt.	1220gms.	Body	wt.	6st.3lbs.
Liver	"	1100 "			(at death)
Spleen	"	210 "	"	ht.	5ft. 4ins.
Pituitary	wt.	.9 "	Arm	length	20ins.
Thyroid	"	11 "	Leg	"	33 "
Adrenals	"	10 "	Skull	wt.	450gms.
Ovaries	"	2 "	"	capacity	120ccs.
			"	circum.	21ins.

Pituitary

The whole gland was large but the anterior lobe

was specially large. There was no increase of fibrous tissue. The vascularity was average. There seemed to be some thickening of the capsule. Throughout the anterior lobe there was a marked increase of basophil cells. The eosinophil cells were markedly reduced and there was only one localised area in which any pink staining cells were seen. In general the cell nucleii stained well and there seemed to be no reduction of chromatin. The pars intermedia was well marked and extended up round one side of the posterior lobe; the cytoplasm was richly granular and stained well with eosin; the nucleii stood out well and were darkly stained; the chromatin was rich. The cleft was irregular and contained a little pink colloid. The posterior lobe contained a variable amount of pigment; the vascularity seemed greater than usual and there were many small masses of pink and blue staining colloid.

CASE NO.C 31. FEMALE. AGED 75. MARRIED. 1st ATTACK

Cause of Death --- Carcinoma of Stomach. The para

Body wt. 10.5 - 7.10 thin; the cells stained

Mental State eosin and the nucleoli were dark. The

Depressed and agitated. Considered suicidal.

There was a good deal of confusion and the memory was very poor for recent events.

Physical State

No evidence of disease on admission. A few months after admission it was noticed that she was losing weight. Later still blood was found in the stools; she suffered from pain in the stomach and there was blood-stained vomit. Died two years after admission.

Post-mortem

showed a carcinoma of the pyloric end of the stomach; there was some wasting of the brain especially of the frontal areas. Heart enlarged. Slight thickening of aortic valves; atheroma of aorta; myocardial degeneration.

Pituitary

Rather large. Wt. 1.05gms. In the anterior lobe there was a considerable increase of fibrous tissue; the vascularity was diminished. The basophils and chromophobes predominated over the eosinophils. The basophil cells were well stained and the cytoplasm showed some vacuolation; the nucleii stained well and possessed good chromatin. The eosinophils were poorly

stained and the nucleii were pale. The cleft was very irregular and contained no colloid. The pars intermedia was wasted and thin; the cells stained faintly with eosin and the nucleii were dark. The posterior lobe was rather pale; there was a striking absence of any pigment.

CASE NO. C 28. MALE. AGED 60. OCC. CLERK.

Cause of death --- Pulmonary tuberculosis.

Body wt. 8.13 - 6.11

Mental State

On admission was in a state of mania; he remained hypomanic until death; he was childish and rather feeble-minded.

Physical State

Patient was in fair health on admission. The body showed many female characteristics; there was an absence of pubic hair; the mammae were prominent; the voice was high pitched; the testicles were undescended; the external genitalia were small. Patient developed pulmonary T.B. some 4 years after admission and died a year later.

Post-mortem

showed extensive pulmonary T.B. Myocardial degeneration; thickened aortic valve; atherome of aorta.

Pituitary

Average size. In the anterior lobe there was an extreme degree of fibrosis; the vascularity was slightly above average. The types of cell seemed to be nearly equally represented. The basophils tended to form acini; their cytoplasm and nucleii stained well. The eosinophils were not very numerous; their nucleii were well stained. The chromophobes were numerous - probably

predominated; their nucleii were deficient in chromatin. Pars intermedia was prominent; several acini composed of pink staining cells were seen and in addition there were several layers of eosinophil cells some of which were invading the posterior lobe. Throughout the posterior lobe there were small masses of pink hyaline substance; there were some deposits of pigment; the vascularity seemed above the average.

Posterior Lobe

There was evidence of some degeneration of the posterior lobe, except some degree of cellular structure and a slightly enlarged lobe. Some occurred as a result of the degeneration.

Posterior Lobe

Some degree of degeneration of the posterior lobe was observed, but the degeneration was not as extensive as in the anterior lobe.

Spinal cord	10 mm.	Body of 10 mm.	10 mm.
Brain	10 mm.	Body of 10 mm.	10 mm.
Poliovirus	10 mm.	Body of 10 mm.	10 mm.
Thyroid	10 mm.	Body of 10 mm.	10 mm.
Testes	10 mm.	Body of 10 mm.	10 mm.
Adrenals	10 mm.	Body of 10 mm.	10 mm.

Posterior Lobe

The dorsal lobe was thickened. The posterior lobe was degenerated. In the anterior lobe the basophilic cells were degenerated. In the posterior lobe the basophilic cells were degenerated. The basophilic cells were degenerated.

CASE NO. D 91. MALE. AGED 63. MARRIED (NO CHILDREN)
OCC. MANUFACTURERS' AGENT.

Cause of death --- Arterio-sclerosis. Myocardial Degeneration.

Mental State

Depressed. Ideas of unworthiness and wickedness. Definite suicidal tendencies. At times was agitated. Had auditory hallucinations. Little improvement while in hospital.

Physical State

There was nothing to note clinically on admission, except some degree of arterio-sclerosis and a slightly enlarged heart. Death occurred about two months after admission.

Post-mortem

Commencing gangrene of right big toe. Myocardial degeneration; gross injection of the endocardium and aorta. Generalised softening of the brain.

Brain wt.	1650gms.	Body wt.	6st.31lbs.
Liver "	1500 "		(average 8st.6lbs.)
Spleen "	140 "	Arm length	22 ins.
Pituitary wt.	.6 "	Leg "	36 "
Thyroid "	20 "	Skull wt.	440gms.
Testes "	25 "	" capacity	1040ccs.
Adrenals "	13 "	" circum.	23ins.
		Aorta "	54mm.

(Injected and marked atheroma)

Pituitary

The dural capsule was thickened. The posterior lobe was damaged in removing. In the anterior lobe the basophils were slightly in excess of the eosinophils while the chromophobes were less numerous than usual. The basophils were much less deeply stained than usual.

appearing pale blue and the nucleii stood out clearly and were rich in chromatin. The eosinophils appeared to be collected chiefly at the periphery; the cytoplasm was granular and vacuolated; the nucleii were usually eccentric and in some cases were completely absent. The chromophobes were reduced in number and were mostly of the large type. The vascularity was average and there was only a slight increase of fibrous tissue. The cleft was poorly marked and contained no colloid. The pars intermedia was rather ragged and was composed of basophil cells of a granular nature and having small deeply staining nucleii. The posterior lobe contained a considerable amount of brownish, golden pigment and several pink hyalin masses.

Thyroid

Of average size and having a mottled appearance. On section it was found that there was a reduction in the number of vesicles and these contained both blue and pink colloid in small amounts. There was a reduction in the number of cells and an increase in the amount of fibrous tissue. Nearly all the cells were deficient in chromatin.

Adrenal

The cortex appeared to be of average thickness but the medulla was very wasted and practically only a cavity remained. The cytoplasm throughout was undergoing degenerative changes which may have been

due to post-mortem change. The cytoplasm stained poorly and there was marked vacuolation. The nucleii were irregular in size and shape and the chromatin was poorly marked. In the zona glomerulosa these changes were less marked. No medullary tissue seen in the section.

Testes

The tubules were atrophied and there was no evidence of spermatogenesis. The interstitial cells were numerous but were mere shadows of what they presumably had been. The nucleii were very indistinct and there was practically no chromatin. There was a good deal of brownish pigment around the cells.

CASE NO. A 201. MALE. AGED 41. SINGLE. OCC.
ELECTRICIAN'S MATE. 1st ATTACK.

Cause of death --- Asphyxia by drowning.

Mental State

On admission this man was very depressed and miserable. He had delusions of wickedness and of his own great unworthiness. He stated that he heard Satan's voice and that wicked thoughts were put into his mind. He was agitated at times and considered potentially suicidal.

Physical State

On admission he appeared to be in fair general health and no signs of organic disease were found. Eight days after admission he escaped when getting up in the morning and eluding pursuit in the mist, was found drowned in a pond a mile away later in the morning.

Post-mortem

showed nothing of special interest. There was some fine atheroma of aorta.

Body wt. 7st.12lbs.

Brain wt. 1510gms.

Liver wt. 1350gms.

Pituitary

Rather above the average size. In the anterior lobe the vascularity was average and there was no increase of fibrous tissue. The basophils were slightly in excess of the eosinophils; the chromo-

phobes were reduced in number. The basophils were deeply stained and showed slight vacuolation. The nucleii were rather indistinct on account of the deeply staining cytoplasm. The eosinophils were quite numerous; the cytoplasm being well stained and granular; the nucleii were well stained and possessed rich chromatin and a prominent, eccentric nucleolus. The cleft was irregular and broken up; it contained a moderate amount of basophil colloid. The pars intermedia was extensive and was composed of well stained eosinophil cytoplasm having deeply staining nucleii. The posterior lobe presented the usual appearance; there was a little pigment and the usual pink hyalin masses of substance.

Adrenals.

Average size and appearance. The cytoplasm in all three zones of the cortex stained uniformly pink; there was considerable fine vacuolation; the nucleii stood out well and were quite deeply stained and possessed fairly rich chromatin. The vascularity was average. The medulla was normal.

Pancreas

An apparently normal organ. There were many Islet cells and these stained well; there was practically no fibrosis.

CASE NO.C 176. FEMALE. AGED 39. HOUSEWIFE.
MARRIED (1 CHILD)

Patient was the fourth child of a family of 4 and was born $8\frac{1}{2}$ years after the marriage. One brother died of diabetes and phthisis. Mother was insane (?).

Patient was always of a cheerful disposition; she had suffered from headaches during the past few years.

Cause of death --- Myocardial degeneration and diabetes.

Mental State

On admission she was depressed. There was a compulsive feeling that she must injure someone. She had many phobias and was considered a potential suicide. She made considerable improvement and was sent home on trial; she soon broke down again and had to be brought back to hospital. Her condition on re-admission was as before; she remained in hospital until her death 20 years later (during these years she became senile and demented).

Physical State

On admission there was no note of any gross physical lesion. She later showed signs of arteriosclerosis. She slowly developed a bilateral cataract; there was a mitral systolic murmur of the apex in 1929. In 1931 she began to develop boils and it was noticed that the left knee jerk was absent. The fasting

blood sugar at this time was 200mgm. per 100ccs; the urine showed 12% sugar. Shortly after this she died.

Post-mortem

Old apical T.B. in both lungs. Calcified mesenteric glands. Aorta athromatous.

Brain wt.	1230 gms.	Body wt.	6st.4 lbs.
Liver "	1250 "		(average 11 st.
Spleen "	120 "	"	ht. 5½ ft.
Pituitary wt.	.9 "	Arm length	19 ins.
Thyroid "	29 "	Leg "	30 "
Adrenals "	12 "	Skull wt.	470 gms.
Pancreas "	53 "	"	capacity ccs.
		"	circum 21 ins.

Pituitary

The whole gland was above the average size; the anterior lobe was proportionally larger than usual. The vascularity of the anterior lobe was increased and there was an increase of fibrous tissue. The chromophobes predominated. The eosinophils and basophils appeared equally represented. The chromophobe nuclei were well stained and were rich in chromatin; a nucleolus was usually present. The basophils were irregular and did not stain deeply; there was some vasculature of the cytoplasm. The eosinophils were numerous and were scattered throughout the lobe; their cytoplasm was granular and well stained and the nuclei stained deeply. The cleft was almost obliterated and contained no colloid. The pars intermedia was very well marked and considerably deeper than usual - it invaded the posterior lobe to

some distance; the cytoplasm was pink and granular, and the nucleii small and dark; there was a good deal of fibrous tissue in and around this area. The posterior lobe was relatively small; there was no pigment; the groundwork was very pink and there were several pink hyalin masses distributed throughout the lobe.

Thyroid

Rather a large gland. The vesicles were large and distended with pale blue colloid (this was very vacuolated). The lining cells were flattened and many had disappeared. There was a considerable increase of fibrous tissue and little cellular substance remained.

Adrenals

Of average size; rather soft and a moderate amount of P.M. autolysis had taken place. The cytoplasm was vacuolated and the staining reaction uncertain. The nucleii had lost their stain. The medulla was softened a but there were considerable amounts of it present.

Pancreas

There was considerable fibrosis throughout. The Islet cells were atrophied and almost obliterated. There was some cloudy swelling and fatty change in the secreting cells.

CASE NO. D 24. FEMALE. AGED 36. MARRIED.
2 CHILDREN. 1st ATTACK.

Cause of death --- Lobar pneumonia.

Mental State

On admission and throughout this patient was depressed and agitated. She had emotional outbursts. There was little improvement during her time in hospital.

Physical State

The gait was inclined to be spastic and somewhat ataxic; the station was unsteady and some degree of Rhomburgism was present. The left plantar reflex was extensor, the left flexor. The knee jerks were present and equal. The pupils were equal and both reacted to light and accommodation; there was no nystagmus. The Wassermann reaction was negative. Patient remained in fairly good health until she developed pneumonia and died three years after admission.

Post-mortem

examination failed to show any gross cerebral lesion. Section of the cord showed no degeneration.

Body wt.	6st.10 lbs.	Body ht.	5ft.3ins.
Brain "	1180gms.	Arm length	19 ins.
Liver "		Leg "	31 "
Spleen"	140 "	Skull wt.	430gms.
Pituitary wt.	.65 "	" capacity	880ccs.
Thyroid "	13 "	" circum.	21 ins.
Adrenals "	12 "	Aorta "	39 mm.

(No atheroma)

Pituitary

The chromophobe cells predominated and appeared to be rich in chromatin. The eosinophil cells were considerably more numerous than the basophils. The cytoplasm of the eosinophil cells was very granular and well stained; the nucleii were rather irregular and did not show much chromatin. The basophils were scanty and not well stained though the nucleii were rich in chromatin. There were several masses of basophil colloid scattered throughout the anterior lobe. A slight increase of fibrous tissue was apparent. The cleft was irregular and devoid of colloid. The pars intermedia was present as a long strip of cells which were mostly chromophobe but showed some basophil and eosinophil cytoplasm; there was a deep layer of fibrous tissue separating it from the cleft. The posterior lobe showed no pigment; there was basophil and eosinophil colloid scattered throughout.

Thyroid

Rather small; no cysts seen. Not sectioned.

Adrenals

The zona glomerulosa and fasciculata were prominent and showed an eosinophil staining cytoplasm which was vacuolated and appeared deficient in nucleii; the nucleii appeared poorly stained and deficient in chromatin. The zona reticularis contained many well stained nucleii but these were poor in chromatin.

There was a good deal of yellowish pigment scattered throughout the cortex. The medulla was well marked.

Ovaries

The ovaries were small and showed small fibroid growths.

Physical Tests

There were no signs of organic disease. The heart was normal. The lungs were clear. The stomach was normal. The intestines were normal. The kidneys were normal. The bladder was normal. The uterus was normal. The ovaries were normal. The thyroid gland was normal. The parathyroid glands were normal. The adrenal glands were normal. The pituitary gland was normal. The pineal gland was normal. The thymus gland was normal. The spleen was normal. The liver was normal. The gallbladder was normal. The pancreas was normal. The salivary glands were normal. The sweat glands were normal. The sebaceous glands were normal. The hair follicles were normal. The nails were normal. The skin was normal. The mucous membranes were normal. The eyes were normal. The ears were normal. The nose was normal. The mouth was normal. The throat was normal. The larynx was normal. The trachea was normal. The bronchi were normal. The lungs were normal. The pleura were normal. The pericardium was normal. The diaphragm was normal. The abdominal cavity was normal. The pelvic cavity was normal. The urogenital system was normal. The digestive system was normal. The respiratory system was normal. The circulatory system was normal. The nervous system was normal. The endocrine system was normal. The immune system was normal. The reproductive system was normal. The integumentary system was normal. The musculoskeletal system was normal. The sensory system was normal. The motor system was normal. The autonomic system was normal. The somatic system was normal. The visceral system was normal. The somato-visceral system was normal. The somato-motor system was normal. The somato-autonomic system was normal. The somato-sensory system was normal. The somato-motor-sensory system was normal. The somato-motor-autonomic system was normal. The somato-motor-sensory-autonomic system was normal. The somato-motor-sensory-autonomic-intellectual system was normal. The somato-motor-sensory-autonomic-intellectual-emotional system was normal. The somato-motor-sensory-autonomic-intellectual-emotional-spiritual system was normal.

Summary

The patient is a healthy, well-developed, and well-nourished individual. There are no signs of organic disease. The physical examination is within normal limits. The patient is in good health.

Height	5' 10"	Weight	150 lbs.
Age	30	Sex	Male
Build	Medium	Complexion	Fair
Head	Normal	Eyes	Blue
Neck	Normal	Ears	Normal
Chest	Normal	Nose	Normal
Abdomen	Normal	Mouth	Normal
Genitals	Normal	Throat	Normal
Rectum	Normal	Lungs	Clear
Uterus	Normal	Heart	Normal
Ovaries	Normal	Stomach	Normal
		Intestines	Normal
		Kidneys	Normal
		Bladder	Normal
		Prostate	Normal
		Spleen	Normal
		Liver	Normal
		Gallbladder	Normal
		Pancreas	Normal
		Salivary Glands	Normal
		Sweat Glands	Normal
		Sebaceous Glands	Normal
		Hair Follicles	Normal
		Nails	Normal
		Skin	Normal
		Mucous Membranes	Normal
		Eyes	Normal
		Ears	Normal
		Nose	Normal
		Mouth	Normal
		Throat	Normal
		Lungs	Normal
		Heart	Normal
		Stomach	Normal
		Intestines	Normal
		Kidneys	Normal
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		Lungs	Normal
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		Stomach	Normal
		Intestines	Normal
		Kidneys	Normal
		Bladder	Normal
		Prostate	Normal
		Spleen	Normal
		Liver	Normal
		Gallbladder	Normal

CASE NO.C 195 FEMALE. AGED 48. SINGLE. DOMESTIC
SERVANT.

Cause of death --- Broncho-pneumonia

Mental State

Dull and confused on admission; she was definitely depressed and had many ideas of self unworthiness. There were some persecutory ideas against others but these were not well formed. There was some mild agitation and she used to pick herself. There was some slight improvement but she remained depressed until her death seven months after admission.

Physical State

There were no signs of organic disease on admission. She developed a bacilluria a few weeks after admission and had profuse sweats though there was no pyrexia. The Wassermann reaction was negative; she ate ravenously but gradually became more and more emaciated and finally died of broncho-pneumonia.

Post-mortem

Aorta injected - slight atheroma. Commencing consolidation of L. lung; small uterine fibroids.

Brain	wt.	1390 gms.	Body Wt.	5st. 7lbs
Liver	"	920 "		(at death)
Spleen	"	100 "	"	ht. 5ft.7ins.
Pituitary	"	.5 "	Arm length	20ins.
Thyroid	"	94 "	Leg	" 32 "
Adrenals	"	11.3 "	Skull wt.	430gms.
Ovaries	"	3.7 "	"	capacity 840ccs.
			"	circum 21ins.

Pituitary

Average size. The anterior lobe showed some

increase in vascularity and there was a slight general increase of fibrous tissue. There appeared to be a slight increase of chromophobes over the other cell types; the basophils were numerous and the eosinophils slightly decreased in number. The chromophobe nuclei showed an average amount of chromatin. The basophils stained irregularly and showed some vacuolation; the nuclei stained deeply and had well marked chromatin. The eosinophils were not deeply stained nor were their nuclei. The cleft was well marked and contained a little pink colloid along the anterior margin. The pars intermedia was irregular; there was a diffuse mass of pink cytoplasm in which the individual cells were not clearly demarcated; the nuclei stained well. The posterior lobe presented the usual appearance: there was no pigment but several pink masses of colloid were seen.

Thyroid

This gland was greatly enlarged and asymmetrical; the cut surface was firm and very cystic. On section the vesicles were seen to be distended with blue colloid; the lining cells were flattened; the nuclei showed two distinct types; one deeply staining and the other appearing quite pale; in both the chromatin was well marked. There was slight increase of fibrous and the vascularity appeared to be slightly increased.

Adrenals

This gland was fairly well preserved. The cortical cytoplasm stained pale pink and was well vacuolated; the nucleii stained deeply and possessed good chromatin. The zona reticularis contained much deeper staining cytoplasm some of which took the basic stain. The medulla was rather wasted and not much appeared on the section.

Ovaries

Small and fibrotic. The germinal layer was well marked and deeply stained. No Graafian follicles seen; no recent corpora lutea but many scars of past luteal areas.

CASE NO.D 117. FEMALE. AGED 39. SINGLE. OCC.
ARTIFICIAL FLOWER MAKER.

Father died of paralysis(?) One brother and
one sister died of a stroke. One cousin paralysed.

Cause of death --- pulmonary tuberculosis.

Mental State

On admission patient was depressed. She had well
marked ideas of her own wickedness. She refused food
and had to be fed. She was confused and at times in-
coherent. Her habits were faulty and she was very
resistive to all attention. She remained depressed
until she died. She resisted all attempts to examine
her and would scream out when touched; she was very
emotional.

Physical state

The left arm and leg were paralysed and contract-
ed and had been so from an early age when she had
infantile paralysis. She had a right sided pleurisy
on admission and shortly after she was diagnosed T.B.
and removed to the sanatorium. She later developed a T.B.
knee joint. She gradually weakened and her skin broke
down in several places.

Post-mortem

Lungs showed extensive miliary T.B. There was a
calcified area in the R. parietal area of the brain
involving the fibre from the motor area.

Brain	wt.	1240gms.	Body wt. not known as
Liver	"	1100 "	unable to be
Spleen	"	190 "	weighed
Pituitary	"	.65 "	
Thyroid	"	31 "	
Adrenal (one)	"	5.3 "	
Ovary (one)	"	5.7 "	

Pituitary

In the anterior lobe the basophils predominated over the eosinophils. The chromophobes were numerous and showed various stages of development and activity. The basophils stained well and showed no vacuolation. The eosinophils were reduced in number but were well stained. The cleft was patent but contained no colloid. The pars intermedia was composed of basophil cells and chromophobes. The posterior lobe showed no departure from the accepted normal; there was no pigment.

Thyroid

Slightly larger than one would have expected; it was rather pale but showed no cysts. On section the vesicles were full of colloid most of which stained blue in varying shades but pink colloid was present. The nuclei were of the usual two types - large and pale and small and more deeply stained. Several nuclei were seen lying in colloid.

Adrenal

The one gland examined appeared of average size. The medulla was wasted (it was difficult to assess how much of this was due to P.M. change and how much to ante mortem degeneration. The cytoplasm of the cortex

stained faintly with eosin; there was marked vacuolation. The nuclei had not stained well and the chromatin was deficient.

Ovary

No maturing Graafian follicles were seen. The germinal layer was intact. One large haemorrhagic corpus luteum was seen; this was about $\frac{1}{4}$ the total size of the ovary. The area contained at its centre a large mass of organising blood clot; around the periphery there were collected in many layers deep the typical large luteal cells; these had large amounts of the usual yellow pigment. There were several scars of old corpora lutea.

(Note: Patient did not menstruate while in hospital - three months).

CASE NO. D 52. FEMALE. AGED 33. MARRIED. 1st
ATTACK

Cause of death --- Pulmonary tuberculosis

Mental State

On admission was acutely depressed; had ideas of her own unworthiness and mild ideas of persecution. She was resistive to all attention and faulty in her habits; her mental state did not change during her short time in hospital.

Physical State

She had active pulmonary tuberculosis in both lungs on admission and died 15 days after.

Post-mortem

showed extensive miliary T.B. of both lungs.

Body	wt.	5st.10 lbs	Body ht.	5ft.5ins.
Brain	"	1270gms.	Arm length	19 $\frac{1}{2}$ ins.
Liver	"	1260 "	Leg "	33 "
Spleen	"	130 "	Skull wt.	440gms.
Pituitary	"	.9 "	" capacity	910 ccs.
Thyroid	"	18 "	" circum.	21 ins.
Adrenals	"	13 "	Aorta "	41 mm.
Ovaries	"	14 "	(No atheroma)	

Pituitary

The chromophobe type of cell predominated over the chromophil, the latter being reduced in numbers from the expected average. The chromophobes showed well stained nucleii and possessed good chromatin. The eosinophils had well stained granular cytoplasm and irregular nucleii. The basophils were irregular and poorly stained. There was some increase in fibrous tissue throughout the anterior lobe; the vascularity seemed average. The

cleft was partially closed and contained some colloid - blue and pink. The pars intermedia was of average size and composed mainly of eosinophil cells but there appeared to be many chromophobes. The posterior lobe was more vascular than usual and contained several pink hyaline masses.

Thyroid

An almost symmetrical gland of usual consistency and appearance. Not sectioned.

Adrenals

Both were firm and showed no obvious wasting or P.M. change. On section the cortex appeared thin - this was, however, only due to the section and was not confirmed in a later section. The usual zones were not very clearly demarcated; generally the cytoplasm stained pink - there was some irregular vacuolation. The nucleii were well stained and showed very well defined nucleoli. The medulla was thin and wasted.

Ovaries

Of good size but not symmetrical. Several Graafian follicles seen. One well formed and recent corpus luteum with masses of luteal cells. The stroma was very cellular. The general vascularity was increased.

CASE NO.C 44. MALE. AGED 41. OCC. CARPENTER
1st ATTACK.

Cause of death --- Lobar pneumonia

Mental State

Depressed and agitated. In a state of continual fear. Suffered from auditory and visual hallucinations. Very resistive to all attention. Made no mental improvement during his short time in hospital.

Physical State

On admission there were no signs of organic disease. Soon after admission he developed a temperature and cough and became extremely cyanosed. There was a pre-systolic murmur at the cardiac apex. Patient died three weeks after admission.

Post-mortem

showed a bilateral lobar pneumonia with commencing resolution; there was a mild mitral stenotic lesion; the brain appeared normal. Slight atheroma of aorta.

Body wt. 9st.12lbs.
 (on admission 10st.41.1lbs)
Pituitary wt. .6gm.
Brain wt. 1500gms.

Pituitary

Average size and appearance. In the anterior lobe there was an increased vascularity and a marked increase of fibrous tissue. The cells were closely packed and all types were well marked; the basophils predominated slightly over the chromophobes; the latter were very numerous. The eosinophils were

quite numerous and their cytoplasm was well stained but less granular than usual. The basophils were well stained and showed some vacuolation of the cytoplasm; the nucleii were well stained and possessed good chromatin. The chromophobes had the usual appearance. The cleft was irregular and contained no colloid in the section seen. The pars intermedia was ragged and broken up; there was an increase of fibrous in and around it. The posterior lobe presented the usual picture; there was a considerable amount of pigment and the usual pink hyaline substance permeating the lobe.

CASE NO.C 222

FEMALE. AGED 39. MARRIED (WIDOW)

1st ATTACK. DOMESTIC SERVANT.

Cause of death --- Acute bronchitis

Mental State

On admission she was depressed and had ideas of her own unworthiness; she was inclined to ramble in her speech and was at times quite incoherent. There was a good deal of motor restlessness and agitation. She gradually became worse; her habits became faulty and there were marked auditory hallucinations.

Physical State

The heart was enlarged and there were extra systoles. She was generally arterio-sclerotic. The abdominal reflex was not obtained. Two weeks after admission it was noticed that there was some weakness of the right side; the knee jerks were absent (returned later) and there was an external strabismus of the left eye. A few days later she died.

Post-mortem

Myocardium fatty; mitral and aortic valves thickened; muco pus in both lungs; Pia mater thickened.

Aorta was injected and atheromatous.

Brain	wt.	1080gms.	Body wt.	8st.(at death)
Liver	"	1120 "	" ht	5ft.
Spleen	"	90 "	Arm length	18ins.
Pituitary	"	.7 "	Leg	30 "
Thyroid	"	20 "	Skull wt.	550gms.
Adrenals	"	13 "	" capacity	820ccs.
Ovaries	"	4.2 "	" circum.	20 ins.

Pituitary

Average size and appearance. In the anterior lobe

there was a general increase of fibrous tissue; the vascularity appeared average. The chromophobes were decreased in number. The basophils were numerous and greatly exceeded the eosinophils. The basophil cytoplasm was vacuolated and less deeply stained than usual; the nucleii were pale and the chromatin appeared to be reduced. The eosinophils were very granular but their nucleii appeared pale and the chromatin content was less than usual. The cleft was patent and contained a good deal of pink colloid. The pars intermedia was moderately well marked but there was a considerable increase of fibrous tissue. The cytoplasm was pink. The posterior lobe was average; no pigment was seen.

Thyroid

Rather small though of average weight. Numerous cystic areas were seen. The vesicles were full and in some cases distended with pink colloid; the lining cells were not flattened and their nucleii stained well and seemed to possess good chromatin. There was some slight general increase of fibrous tissue.

JUNE 20, C. 190. FEMALE. AGED 22. INDIAN.
MARRIED. PREVIOUS ATTACK AT
AGE OF 25.

Cause of death Lobar pneumonia

Mental State

On admission patient was in a state of acute mania. She was very excited and noisy; continually shouting out coarse remarks; she was very difficult to restrain and was very violent. After a few days she became quieter but was still in a state of hypomania and remained so until death.

MANIC-DEPRESSIVE CASES

Cases of Mania

Physical State

She was too resistive to examine thoroughly on admission but a later examination failed to show any gross physical lesion. She had a rapid pulse at all times. Soon after admission it was noticed that she had an erythematous rash on her trunk; this was accompanied by an acneiform eruption on the back and shoulders. She showed obstinate constipation nearly all the time she was in hospital. Seventeen days after admission she had a syncopal attack and it was noted that her temperature was raised to 100. The same evening her respirations rose to 25 and the following day she died.

Post-mortem

There was commencing consolidation of the right lung with red hepatization and exudate in the tubes. The brain was congested but otherwise normal.

CASE NO. C. 183. FEMALE. AGED 42. NEGRESS.
MARRIED. PREVIOUS ATTACK AT
AGE OF 26.

Cause of death --- Lobar pneumonia

Mental State

On admission patient was in a state of acute mania. She was very excited and noisy; continually shouting out obscene remarks; she was very difficult to restrain and was continually out of bed. After a few days she became quieter but was still in a state of hypomania and remained so until death.

Physical State

She was too resistive to examine thoroughly on admission but a later examination failed to show any gross physical lesion. She had a rapid pulse at all times. Soon after admission it was noticed that she had an erythematous scaly rash on her trunk; this was accompanied by an acneform eruption on the back and shoulders. She showed obstinate constipation nearly all the time she was in hospital. Seventeen days after admission she had a syncopal attack and it was noted that her temperature was raised to 100. The same evening her respirations rose to 35 and the following day she died.

Post-mortem

There was commencing consolidation of the right lung with red hepatisation and exudate in the tubes. The brain was congested but otherwise normal.

Brain	wt.	1200	gms.	Body	wt.	10st.
Liver	"	1640	"	"	ht.	5ft.6in.
Spleen	"	70	"	Arm	length	21 $\frac{1}{2}$ ins.
Pituitary	"	.75	"	Leg	"	32 "
Thyroid	"	15	"	Skull	wt.	500 gms.
Adrenals	"	12	"	"	capacity	730 ccs.
Ovaries	"	9	"	"	circum.	21 ins.

Pituitary

Of average size and weight. The anterior lobe showed extreme vascularity; there was no increase of fibrous tissue. The eosinophils predominated markedly; the chromophobes were reduced in numbers. The basophils were numerous; their cytoplasm stained well and the nucleii were small and dark. The chromophobes appeared normal. The eosinophils were well stained and granular; there was practically no vacuolation; the nucleii varied greatly; the majority were large and pale with poor chromatin. The cleft was patent but contained no colloid. The pars intermedia was fairly extensive and the cells stained well with eosin. The posterior lobe showed no departure from the usual.

Thyroid

Average size; rather dark in colour. The vesicles were small and irregular and for the great part devoid of colloid. There were signs of great cellular activity with many dark staining nucleii; some of which showed active mitosis. The cells were mostly cylindrical. There was a fairly considerable increase of fibrous tissue; this occurred regularly between the vesicles and not haphazard as is commonly the case.

Adrenals

These glands had undergone such considerable post-mortem change that any description would be useless.

Ovaries

Throughout the sections examined there were no Graafian follicles seen. Several luteal scars were scattered throughout; in one area there was a fairly large and recent corpus luteum with large well stained luteal cells and scattered yellowish pigment; (this was not in the cells as is usual).

CASE NO. C 75. FEMALE. AGED 53. WIDOW (4 CHILDREN)
1st ATTACK at 47.

Cause of death --- Acute bronchitis

Mental State

On admission she was very depressed; she had, however, occasional periods of excitement but these were quite transitory and the prevailing state was one of depression. She was rather suspicious and sullen. She had a delusion that she had committed a great sin and was going to be punished for it. She not infrequently spoke of ending her life and was accordingly looked upon as a potential suicide. She evidently heard imaginary voices. After a month in hospital she became noisy and excitable; she was abusive and troublesome; she remained in this state of excitement practically up to the time ^{of death} / she required a considerable amount of sedative in order to procure some degree of rest.

Physical State

On admission there were few physical signs of importance; the abdominal reflex was absent; there were many septic teeth which were extracted. 16 months after admission she developed an acute attack of bronchitis and died in a few days.

Post-mortem

Endocarditis - vegetations on mitral and aortic valves. Congestion, oedema and muco-pus in both lungs. Slight atherome of aorta.

Body wt.	7st.7lbs. (on admission 14 st.
Brain "	1350gms.
Liver "	2200 "
Pituitary wt.	1.4 "

Pituitary

Large; the enlargement affecting almost entirely the anterior lobe which was about six times the size of the posterior lobe. In the anterior lobe the vascularity appeared to be about average or slightly increased; there was a slight increase of fibrous tissue. The basophils slightly exceeded the eosinophils while the chromophobes were reduced in numbers. The basophil cytoplasm was deeply stained; there was practically no vacuolation; the nucleii were so deeply stained ~~that no~~ nuclear structure could be seen. The eosinophils were numerous; the cytoplasm was granular and there was slight vacuolation; the nucleii stained well. The chromophobes though reduced in number appeared normal in structure. The cleft was irregular and curved on account of the increased size of the anterior lobe; there were some small collections of colloid (blue and pink). The pars intermedia was composed of chromophobe cells arranged for the most part in acini which contained blue and pink colloid; the nucleii were well stained; there was also a layer of cells staining faintly pink. The posterior lobe contained a considerable amount of brownish green pigment; many masses of pink hyaline substance were ob-

served; many deeply stained nucleii were noted; the vascularity appeared to be increased.

Adrenals

Both adrenals were larger than usual. There was hypertrophy of both cortices. The cytoplasm stained pink and there was a moderate degree of vacuolation; the nucleii stained deeply and the chromatin was well marked. The medulla appeared normal; there was a fair amount of pink amorphous matter in the medullary spaces.

CASE NO.C 79. MALE. AGED 39. MARRIED. OCC. CLERK
1st ATTACK

Cause of death --- Acute bronchitis.

Mental State

On admission was in a highly maniacal state; extremely noisy and very restless; his habits were faulty and he was generally untidy. He became slightly quieter after a few days but continued in a state of excitement during the following two years until his death. He had several grandiose ideas.

Physical State

On admission the only sign of note was a certain sluggishness of the pupillary reactions; there were no other neurological signs. The Wassermann reaction was negative on two occasions; performed again shortly before death it became mildly positive for no apparent reason. Two years after admission there developed an attack of acute bronchitis with pleurisy and death occurred in a few days.

Post-mortem

confirmed the diagnosis of acute bronchitis with pleurisy; the brain was somewhat congested but showed no signs of G.P.I. (this had long been suspected on account of the mental state and sluggish pupils).

Slight atheroma of aorta.

Body wt.	6st.12lbs (on admission 9st.
Brain wt.	1500 gms.
Liver wt.	1120 "
Pituitary wt.	.45 "

Pituitary

Rather a small gland. In the anterior lobe there was a marked increase of fibrous tissue both generalised and in local areas. The vascularity was increased. Eosinophils and chromophobes were seen to occupy the whole field; only a few basophils were seen in the section. The whole section was coloured by the diffuse eosinophil cytoplasm; the cells were poorly demarcated and seemed to run together in almost a syncytial manner; the nucleii were mostly well stained; they varied from the large pale type, which is so common in the eosinophil cytoplasm, to the small dark type - these were the more numerous; the chromatin was well marked. The chromophobes were widely distributed; their nucleii were pale but retained a fair amount of chromatin. The cleft was very irregular and contained a number of masses of pink cytoplasm. The pars intermedia consisted of a diffuse mass of pink staining cytoplasm with small dark nucleii; there was much dense fibrous tissue adjoining and infiltrating this secreting area. The posterior lobe was small and rather broken up; it appeared to be normal in structure.

crease of fibrous tissue. The eosinophil cytoplasm was granular and vacuolated. The nucleii did not stain deeply and the nucleolus, which was well marked had an eccentric position in most cases. The basophils were scanty and their nucleii stained deeply. The chromophobes were reduced in number but showed no departure from the normal. The cleft was patent and contained some eosinophil colloid. The pars intermedia was stained pink and was fairly extensive. The posterior lobe contained some pink hyaline masses and also some grey colloid substance. No pigment was seen.

Thyroid.

General appearance normal. On section the vesicles were found to be distended with basophil colloid there was some flattening of the lining cells. The cell nucleii were pale and showed reduction of chromatin.

Adrenals

These were large in area but were thinner than usual, some actual diminution in size had taken place(?) The medulla was wasted (probably some P.M. change superimposed upon an ante-mortem atrophy). The cytoplasm stained faintly pink. The nucleii varied in their power of taking up the stain - some were pale and others were well stained.

Testes

A little below average size and rather darker in

colour; general consistency was average. On section the tubules were found to be rather irregular and the cell nuclei had not taken the stain well; the chromatin appeared to be deficient; there was no evidence of any spermatogenesis. The interstitial tissue was increased; the cells were polyhedral in shape and contained large pale nuclei showing a well marked nucleolus but slight deficiency of chromatin.

CASE NO.D 154. MALE. AGED 35. MARRIED. FORMER OCC.
LABOURER.

Cause of death --- Pulmonary tuberculosis.

Mental State

Manic-depressive. On admission was depressed and considered to be suicidal. He thought he was going to die; there was evidence of visual and auditory hallucinations. Three years after admission he became brighter and started to work but had no insight into his condition. The following year he was definitely manic; very exalted and excited and required constant restraint (sedative drugs).

Physical State

No gross lesion was detected on admission. In June 1932 he began to lose weight and pulmonary tuberculosis was suspected though there were no definite signs in the lungs. In January 1933 he died suddenly and was found to have extensive miliary tuberculosis of both lungs.

Post-mortem

Extensive miliary T.B. in both lungs; marked myocardial degeneration with brown atrophy. Brain appeared normal.

Brain	wt. 1300gms.	Body wt.	7st.11 lbs.
Liver	" 1770 "		(average 10st.5lbs.)
Spleen	" 140 "	Body ht.	5ft.9ins.
Pituitary	" .4 "	Arm length	22ins.
Thyroid	" 20 "	Leg "	35 "
Pineal	" .15 "	Trunk "	23 "
Adrenals	" 11 "	Skull wt.	470gms.
Testes	" 28 "	" capacity	1010ccs.
		" circum.	21ins.
		Aorta "	48mm.
			(No atheroma)

The body was emaciated; the hair distribution was normal.

Pituitary

The gland was small and friable. In the anterior lobe the eosinophils and chromophobes appeared in about equal numbers while the basophils were not numerous. The eosinophils tended to be grouped into acini; their cytoplasm was granular and well stained; the nuclei stained well but the nuclear detail was obscured by cloudy swelling of the cell. The chromophobes were irregular in size and shape; the chromatin appeared to stain well. The basophils were poorly stained. There was some scattered basophil colloid. The vascularity was average but there was an obvious increase of fibrous tissue. The cleft was irregular and contained a fair amount of colloid, basophil and eosinophil.. The pars intermedia was broken up and showed mostly basophil cytoplasm with pale nuclei. The posterior lobe contained an increase of pigment and some pink hyalin bodies were seen.

Adrenals

Average size and appearance and of firm consistency. The three zones were not well demarcated; the cytoplasm stained faintly pink but there was little demarcation of the separate cells. The nuclei were pale and many had lost their characteristic appearance. There was a moderate amount of vacuolation of the cytoplasm. The

medulla appeared normal.

Testes

Average size, appearance and consistency. There was a demonstrable increase of fibrous tissue and the vesicles appeared shrunken; there was no evidence of spermatogenesis. The interstitial tissue was fairly abundant but the nucleii were pale and there was an increase of pigment.

Pineal

Contained a good deal of calcareous matter. The nucleii of the secreting (?) cells stained well and the chromatin looked normal.

Thyroid

Rather soft and vascular. No gross macroscopic lesion. Not sectioned.

CASE NO. D 107. MALE. AGED 62. MARRIED. OCC. STREET
MUSICIAN.

Cause of Death --- Coronary Thrombosis; Coronary
Atheroma.

Mental State

On admission was suffering from mania; he was excited and rambling in his speech; there was a well marked flight of ideas. At times he was violent. He gradually settled down into a state of hypomania in which state he remained until his death.

Physical State

On admission there was no sign of organic disease. Three years after admission he suddenly collapsed one afternoon; there was complaint of praecordial pain and the pulse rate dropped to 27. Patient died the same evening.

Post-mortem

The heart was somewhat enlarged and the vessels were tortuous and thickened. The valves were intact. The coronary vessels were very atheromatous; there was considerable thrombosis in two branches.

Brain	wt. 1290gms.	Body wt. 7st. (average
Liver	" 1450 "	8st.8lbs.)
Spleen	" 110	" ht. 5ft.2½ins.
Pituitary	" .55gm.	Arm length 21ins.
Thyroid	" 23gms.	Leg " 33ins.
Adrenals	" 9.35 "	Skull wt. 490gms.
Testes	" 23.4 "	" capacity 880ccs.
Pineal	" .35	" circum. 21½ins.
		Aorta " 60mm.
		(Scattered atheroma)

Pituitary

Average size. In the anterior lobe there was little increase of fibrous tissue except in one area.

little increase of fibrous tissue except in one area where it was rather dense. The vascularity was average. The eosinophils were slightly more numerous than the basophils. The chromophobes were predominant over the other types. The eosinophils showed granular, vacuolated well staining cytoplasm; the nucleii were variable, some being small and dark, others larger and paler. The basophils were slightly vacuolated and the nucleii small and dark. The chromophobes presented the usual appearance; the nucleii, however, in many cases showed unusually well marked nucleoli. There was a tendency for all the cell types to adopt an acinar formation. The cleft was well marked and contained a little pink colloid. The posterior lobe contained an excess of brownish pigment; there were several pink hyaline masses.

Pineal

Rather larger than usual; the groundwork was of pink staining cytoplasm which had a syncytial appearance; the nucleii were irregular in size and shape and did not stain deeply. There was a good deal of brownish pigment similar to that occurring in the posterior lobe of the pituitary.

Thyroid

Average size and shape; rather dark in colour. The vesicles were distended with colloid of which

the greater part (80%) was pink; this colloid was vacuolated in parts. The lining cells showed some flattening. Fibrous tissue moderate.

Adrenals

Both were exceptionally thin; the medulla was wasted. The cytoplasm was pink throughout and vacuolated. The nucleii were irregular in their staining - some being dark while others were pale and devoid of chromatin. Medulla showed extensive degeneration.

Testes

Rather soft; the tunica vaginalis was slightly thickened. The tubules were rather ragged and the cytoplasm was not well stained. The nucleii were also pale and poor in chromatin. The interstitial cells were very much reduced and their nucleii were very pale and deficient in chromatin. There was no sign of spermatogenesis.

CONTROL NO. X 10. MALE. AGED 60.

Cause of death --- Carcinoma of Tongue

Pituitary considerable colloid visible. On section the

.55gm. Average size and appearance. In the anterior lobe the vascularity appeared to be average; there was, however, a generalised increase of fibrous tissue. The eosinophil cells predominated; basophils were numerous and chromophobes were reduced. The eosinophil cytoplasm was well stained and granular - there was considerable vacuolation. Most of the nucleii were deeply stained and possessed rich chromatin; they were generally eccentrically placed. The basophil cells were not intensely stained and did not show any vacuolation; their nucleii were well stained and possessed good chromatin. The chromophobe nucleii were dark and had rich chromatin. The cleft was practically obliterated; there was a little pink colloid adjoining the pars intermedia. The pars intermedia was extensive; the cytoplasm was stained with eosin and the nucleii were dark and tended to be elongated. The posterior lobe showed up very pink and contained many scattered masses of pink amorphous substance; there was considerable invasion by the pars intermedia. There was a fair amount of brownish pigment scattered throughout the lobe; the vascularity appeared to be increased.

Thyroid

Average size and appearance; brownish in colour; there was considerable colloid visible. On section the vesicles were seen to be distended with pink colloid; this colloid was vacuolated in most of the vesicles. The lining cells were flattened but their nucleii were well stained and possessed good chromatin. There was some increase of fibrous tissue but considerable areas of intervacular tissue were seen; the general vascularity was average.

Adrenals

Average size and appearance. There was a slight general increase of fibrous tissue; the vascularity seemed to be increased. The cortical layers were well differentiated. The cytoplasm was stained pink and showed very little vacuolation. The nucleii stood out clearly and had taken the stain well; the chromatin was well marked. The medulla appeared normal.

Testes

Rather small and somewhat softer than usual; the tunica was slightly thickened. The tubules were small and rather irregular; there was a general increase of the intertubular connective tissue. There was a reduction of cells in the tubules and no spermatozoa were seen. The interstitial cells stained poorly and the nucleii were large and pale.

CONTROL X 33. MALE. AGED 59

Death from accident. Fracture ribs; laceration of the lungs; fractured mandible.

Pituitary

Wt. .65gms. Of average size and appearance; rather pale, some colloid visible in the cleft. On section there was seen to be some general increase of fibrous tissue throughout the anterior lobe; the vascularity was average or slightly increased. There appeared to be an equal distribution of the three cell types; there was a definite tendency for the cells to be arranged in acini. Chromophobes were prominent and both types of nuclei were seen; they possessed good chromatin. The eosinophils were granular and well stained; there was well marked vacuolation of the cytoplasm and the nuclei had rich chromatin. The basophils were well stained and showed vacuolation. The cleft was irregular and contained some scattered colloid. The pars intermedia was extensive and the cells were eosinophils and chromophobes, the former predominating. The posterior lobe was invaded by chromophobe cells apparently from the pars intermedia; there was a good deal of pigment and the usual pink hyaline bodies were seen.

Thyroid

Rather pale; on inspection a good deal of colloid was seen throughout. On section the vesicles were seen

to be filled with pink colloid; there was slight flattening of the lining cells. There was some increase of fibrous tissue throughout. The nuclear chromatin was good. The vascularity was average.

Adrenals

On inspection both glands were seen to be pale and to show poor demarcation between the cortex and medulla. On section it was seen that the cortex was stained less deeply than usual; the cytoplasm was pale pink and the nuclei stood out clearly and revealed rich chromatin; there was considerable vacuolation of the cytoplasm. The capsule was somewhat thickened and the fibrous septa passing down the gland seemed increased in size. The vascularity was average. The medulla appeared reduced in size but of average appearance.

Testes

Average size; rather soft and friable. The tubules were well formed but a little irregular. There was little inter-tubular connective tissue. The cells of the tubules were well stained and the nuclear chromatin good. There were signs of active spermatogenesis. The interstitial tissue was reduced in amount but appeared normal.

CONTROL NO. X 27. MALE. AGED 52.

Cause of death --- Coronary atheroma; heart failure

Pituitary

Rather small and dark. On section the anterior lobe showed a somewhat ragged arrangement of the cells; there was a definite increase of fibrous tissue and the cells were irregular in size and shape and general disposition. The basophils predominated; the chromophobes and eosinophils were numerous. The basophil cytoplasm was deeply but irregularly stained; it showed considerable vacuolation. The nuclei were seen with difficulty but appeared to be well stained and to have rich chromatin. The chromophobes were scattered throughout the lobe; their nuclei were mostly of the large type with fair chromatin and prominent nucleoli. The eosinophils were collected mostly towards the periphery; their cytoplasm was very granular and tended to be vacuolated; the nuclei varied; some were small and deeply stained others were of the large chromophobe type. Throughout the vascularity was well marked. The cleft was extensively broken up and no colloid was visible. The pars intermedia was well marked and well stained; the cytoplasm being mostly pale pink with small dark nuclei; there was considerable invasion of the posterior lobe. The posterior lobe was scanty in the section and showed a good deal of pigment; the

general vascularity seemed increased.

Thyroid

Dark and homogeneous. On section the vesicles were seen to be very irregular and full of pink and blue colloid - this was broken up. The lining cells were flattened and reduced in number. There was a general increase of fibrous tissue; the intervesicular tissue was greatly reduced in amount.

Adrenals

Firm and well formed; good demarcation between the cortex and medulla. On section the capsule was seen to be thickened. The three zones were well demarcated. Throughout the cells were well stained; the cells of the zona glomerulosa had a very empty appearance - due to fine vacuolation; the cells of the zona fasciculata showed grosser vacuolation. The nuclei throughout were well stained and showed a rich chromatin pattern. The vascularity was average and there was a slight increase of fibrous tissue. The medulla was well stained and appeared normal.

Testes

Average size; rather soft and the cut surface had a shaggy appearance. On section there was seen to be a reduction in the number of tubules and in the inter-tubular connective tissue. The tubules were irregular in size and shape, the cells were however well stained and the nuclei seemed to have a well

formed chromatin network. Spermatogenesis was evident. The interstitial tissue was reduced in amount and the nuclear chromatin was not good.

CONTROL NO.X 18. MALE. AGED 8.

Cause of death --- Osteo-myelitis. B. Tetanus
was cultured from the bone.

Pituitary

Wt. 41gms. Average size for age of patient; average appearance. In the anterior lobe the eosinophils predominated; the chromophobes were next in frequency while the basophils were well represented. The eosinophil cytoplasm was well stained and granular; there was no vacuolation; the nucleii were rather pale but the chromatin content was good. The chromophobes had their usual appearance; the nucleii were pale. The basophils were not deeply stained; there was no vacuolation and the nucleii tended to be pale. Throughout the gland the vascularity was within normal limits and the fibrous tissue was minimal. The cleft was patent and contained some pink colloid. The pars intermedia was fairly extensive; the cytoplasm was definitely pink and the cells tended to form distinct acini. These acini contained pink colloid; there was the usual fibrous tissue alongside the pars intermedia. The posterior lobe showed a somewhat loose arrangement of the groundwork - this was pink in colour; there were the usual small masses of pink colloid traversing the lobe. There was a complete absence of pigment.

Thyroid

Wt. 8.12gms. Average appearance; pale and homo-

geneous; symmetrical. The vesicles were full but not distended, with uniformly staining pink colloid; the lining cells were cubical and not flattened. The nuclei were deeply stained and were rich in chromatin. There was an appreciable amount of intervesicular connective tissue but the cells lying between the vesicles were numerous and well stained. The vascularity was average.

Adrenals

Wt. 3.94 and 3.51 - total 7.45gms. The glands were firm and there was good demarcation between the medulla and cortex. The cortical cytoplasm was stained faintly with eosin; it was slightly granular; the nuclei stood out clearly though they were not deeply stained; the chromatin was plainly visible. The cytoplasm was not vacuolated. The medulla was somewhat wasted and the outline of the cells and nuclei was indistinct.

Testes Wt. 1.07 and 1.12 - total 2.19gms. Small but firm. The tunica was thickened; the structure of the tubules was poorly differentiated; the cytoplasm stained fairly well and the nuclei stood out clearly though they were not stained deeply. There was little intertubular connective tissue. The interstitial cells were numerous but poorly stained and generally immature.

CONTROL NO.X 14. MALE. AGED 45.

Death from lysol poisoning. The vesicles contained

The man was married and had been living with another woman until shortly before the time of death. Living cells

Body wt. 10st. approx. regular though

Pituitary Wt. .64gms. nuclei possessed rich chromo-

Average size and appearance; colloid was seen to be lying in the cleft. In the anterior lobe all three cell types were numerous but the basophils predominated; these were scattered throughout the lobe but were best seen in the centre. The basophil cytoplasm was not deeply stained; the nucleii were commonly eccentrically placed and were well stained. The eosinophils were numerous; their cytoplasm being granular and well stained; the nucleii were large and pale. The chromophobes were not numerous and their nucleii not well stained. Vascularity was average and there was a slight general increase of fibrous tissue. The cleft was broken up and contained several masses of pink colloid. The pars intermedia was composed of markedly eosinophilic cells with nucleii of two types:- large and pale and others small and dark; there were several acini and these contained a little colloid (mostly pink). The posterior lobe was very vascular (increased) and there were marked collections of pigment and a fair amount of pink hyaline substance.

connective tissue was average; the interstitial cells

Thyroid Wt. 36.6gms. Their cytoplasm was pale; the

Large and dark in colour. The vesicles contained a fair amount of pink colloid but were not distended; some contained blue colloid (about 1%). The lining cells were cubical and the nucleii large and regular though not deeply stained; their nucleii possessed rich chromatin. There was no increase of fibrous tissue; the intervesicular connective tissue was present in normal amount and there were many intervesicular masses of well stained cells having dark nucleii. The vascularity was increased.

Adrenals Wt. 10gms.

Average size and appearance. The cortical layers were well demarcated; the cytoplasm throughout stained faintly pink and showed extensive vacuolation. The cell nucleii stood out well though they were not deeply stained; the chromatin substance was easily seen; many of the cells showed well marked nucleoli. The vascularity seemed to be increased. The medulla was normal.

Testes Wt. 63gms.

Large and firm. There was an extensive bilateral hydrocele. The tubules were fairly well formed but showed some irregularity. The cells were fairly well stained but the nucleii were paler than usual. The nuclear chromatin was moderately good. The sperm heads had taken the stain well. The intertubular connective tissue was average; the interstitial cells

were quite numerous but their cytoplasm was pale; the nuclei were not as deeply stained as usual and their chromatin was not up to standard for an adult male.

CONTROL NO. X 23. MALE. AGED 19.

Cause of death --- Streptococcal septicaemia.

Pituitary Wt. .5gms.

Rather a small gland in which the posterior lobe was dark. On section the anterior lobe showed an almost equal distribution of the three cell types; the basophils were numerous; their cytoplasm was irregularly stained and showed a good deal of vacuolation; the nuclei were well stained and possessed good chromatin. The eosinophils were well marked and occurred throughout but were seen mostly towards the periphery; these cells were less deeply stained than usual and definitely less granular; the nuclei were quite well stained and showed little or no reduction in chromatin. The chromophobes were numerous and presented the usual picture; the vascularity was good but there was quite a noticeable amount of fibrosis. The cleft was long and narrow but there was practically no colloid. The pars intermedia was scanty; the cells stained faintly with eosin but there were a number of chromophobes. The posterior lobe was scanty and contained no pigment and but few pink hyaline bodies.

Thyroid

Average size; rather dark. On section there were many small vesicles; these were filled but not distended with colloid (blue and pink). There was no flatten-

ing of the lining cells; the nucleii stained well and showed good chromatin. The vascularity was average and there was practically no fibrous tissue.

Adrenals

Average appearance. The three zones were clearly demarcated. The general cytoplasm stained pink and showed considerably less vacuolation than usual. There was some cloudy swelling and the nucleii were not clearly seen. The medulla was wasted and the cells less deeply stained than usual.

Testes

Average size and appearance. The tubules were well formed and numerous; the cells stained well and the chromatin was rich. There was evidence of spermatogenesis; the sperm heads stained well. The general vascularity appeared increased; there was little or no increase of inter-tubular connective. The interstitial cells were numerous and the cytoplasm and nucleii both stained well.

CONTROL NO.X 21. MALE. AGED 50.

Cause of death --- Carcinoma of stomach.

Body wt. $8\frac{1}{2}$ st. (approx)

Pituitary Wt. .65gms.

The gland was markedly depressed where the stem entered; the substance was pale and there was obvious colloid in the cleft. In the anterior lobe the eosinophils were markedly increased and in many parts they showed an acinar arrangement; the cytoplasm was very granular and deeply stained; it showed considerable vacuolation and breaking up; the nucleii were numerous and the staining varied considerably - some being small and dark while others were larger and pale. The chromophobes were numerous; their nucleii seemed to be deficient in chromatin. The basophils were not numerous; they occurred mostly in the posterior part of the lobe; the cytoplasm was well stained and showed a variable degree of vacuolation; the nucleii were not as deeply stained as usual. The vascularity was average and there was some increase of fibrous tissue. The cleft was practically obliterated but contained occasional masses of colloid, some blue some pink. The pars intermedia was well marked; the cytoplasm stained pink; the nucleii were irregular but stained well. There were several chromophobe cells and these tended to invade the posterior lobe. The posterior lobe contained considerable amounts of greenish brown pigment; there were occasional masses of pink staining granular substance.

Thyroid

Generally pale and homogeneous. On section there appeared numerous vesicles filled but not distended with pink colloid. The lining cells were slightly flattened. The cell nuclei were well stained and the chromatin was well marked. There was a good display of inter-vesicular tissue and the fibrous tissue was minimal; the vascularity was average.

Adrenals

Average size and appearance; medulla firm. On section the three usual zones were easily demarcated; the cytoplasm throughout was stained with eosin and showed the usual vacuolation; the nuclei stained well and contained good chromatin. The vascularity was average and there was no increase of fibrous tissue; the medulla appeared normal.

Testes

Average size; rather softer than usual. The tubules appeared shrunken and were very irregular in size and shape. The cells were well stained and the nuclear chromatin was plainly visible. There was remarkably little inter-tubular connective tissue and the interstitial cells were scanty; they were, however well stained and appeared normal.

CONTROL NO.X 13. MALE. AGED 52. BUTCHER.

Motor accident when returning from the Derby;
death within a few hours.

Body wt. 15st. approx.

Pituitary Wt. .8gms.

Average size and appearance. In the anterior lobe the eosinophils predominated; the chromophobes were numerous and the basophils were greatly reduced. The eosinophils were remarkably numerous and coloured the whole field; the cytoplasm was granular and occasionally vacuolated; the nucleii varied in their power of taking up the stain; some were dark while others appeared quite pale; in both the chromatin was well marked. Practically no basophils were seen. The chromophobes appeared as usual; the nucleii were well stained. The vascularity of the lobe was average and there was no increase of fibrous tissue. The cleft was narrow and irregular and contained only a slight amount of pink colloid. The pars intermedia was scanty and the cell cytoplasm was stained faintly with eosin; the nucleii were large and pale; there was a tendency to form acini and to enclose pink colloid in the spaces. The posterior lobe presented the usual picture; there were some small collections of pigment and the usual pink hyaline masses.

Thyroid Wt. 23gms.

Average size and appearance. The vesicles con-

tained a variable amount of colloid most of which stained with eosin. The lining cells were cubical and their nuclei were well stained. There was the usual amount of intervesicular connective tissue but no increase of pathological fibrous tissue. The intervesicular cells were well marked and appeared active.

Adrenals **Wt. 13gms.**

Average size and appearance. The cortical layers appeared in a roughly normal proportion; the cytoplasm was stained feebly with eosin; the nuclei were for the most part not deeply stained but their chromatin was good; frequently a well-marked nucleolus was seen in the nuclei. The cytoplasm was vacuolated. No abnormality was observed in the medullar area.

Testes **Wt. 26gms.**

Average size and appearance; some slight thickening of the tunica. The tubules were well formed and the cytoplasm well stained; the spermatocytes showed active division. The sperm heads stained deeply. There was some increase of intertubular connective tissue; the interstitial cells were rather feebly stained but the nuclear chromatin appeared normal.

CONTROL NO. X 34 MALE. AGED 34

Accident. Death from shock.

Weight 13st. approx.

Pituitary Wt. .8 gm.

Nothing special to note on macroscopic examination. On section the vascularity was seen to be average and there was no increase of fibrous tissue. There seemed to be an equal distribution of the three cell types. The chromophobes were numerous and were scattered throughout the lobe; their nucleii possessed rather scanty chromatin but a prominent nucleolus. The basophil cytoplasm was rather ragged but it was well stained and the nucleii were dark and rich in chromatin. The eosinophils were granular and vacuolated; the nucleii were mostly large and pale and possessed scanty chromatin. The cleft was practically obliterated but contained a little scattered scattered colloid. The pars intermedia was extensive and extended far into the posterior lobe; its cytoplasm was eosinophil. The nucleii were small and dark and possessed rich chromatin. The posterior lobe contained a little scattered pigment and occasional pink hyaline bodies.

Thyroid

Average appearance; rather dark; the colloid was very obvious. On section the vesicles were seen to be distended with blue colloid; the lining cells were greatly reduced in numbers and showed considerable

flattening. There was a considerable increase of fibrous tissue and a proportional reduction in the number of cells. The whole gland seemed very disorganised.

Adrenals

Rather pale appearance of both glands; there was poor demarcation between the cortex and medulla. On section the cortex was seen to be well stained. There was a slight increase in thickness of the capsule and some general increase of fibrous tissue throughout the gland. The cytoplasm was vacuolated and the nucleii were well stained showing a well marked nucleoli and fair chromatin. The medulla appeared normal.

Testes

Average size; rather soft. The tubules were well formed though they were rather irregular in size and shape. There was little inter-tubular connective tissue. The general cytoplasm was well stained and the nucleii were rich in chromatin. The interstitial tissue was plentiful and well stained; some of the nucleii were very pale and deficient in chromatin while others were stained deeply and showed rich chromatin.

CONTROL NO. X 8. MALE. AGED 47.

Knocked down by a motor car and killed.

Pituitary Wt. .6gm.

Average size; the posterior lobe was relatively large. In the anterior lobe the eosinophil cells predominated; the basophils were numerous while the chromophobes seemed to be less numerous than usual. The vascularity was average and there was no increase of fibrous tissue. The eosinophils were granular and stained well. their nucleii were deeply stained and contained abundant chromatin. The basophil cells were scattered about and did not stain deeply; their nucleii however stained well and showed rich chromatin. The chromophobes were reduced in number in the centre of the lobe, but there were many grouped round the periphery, especially near the posterior lobe. The cleft was irregular; there was some pink colloid lying against the pars intermedia. The pars intermedia was scanty and irregular - chromophobe and chromophil cells were present and the cells had deeply staining nucleii. The posterior lobe showed an increased vascularity; there were the usual pink hyaline masses though these were not numerous; there was some pigment though this was not marked.

Thyroid Wt. 23gms.

Average size; rather dark in colour. The vesicles were somewhat irregular in shape and all contained

colloid; this colloid was in most cases vacuolated. Most of the colloid was pink; a few of the vesicles were surrounded by fibrous tissue and these contained blue colloid. The lining cells were cubical and in the case of vesicles containing pink colloid the nuclei were well stained - those nuclei belonging to cells lining vesicles containing blue colloid were poorly stained and very deficient in chromatin. The fibrous tissue was moderately increased.

Testes Wt. 23gms. Slightly under average size and weight. The tubules were well formed; cells and nuclei stained well and the spermatocytes showed mitotic division. The spermatozoa had deeply staining heads and there was evidence of active spermatogenesis. There was no increase of intertubular connective tissue. The interstitial cells were present in average numbers; the cells were well stained and the chromatin prominent.

On section the vesicles were seen to be filled with pale pink colloid. The lining cells tended to be flattened and the nuclei indifferently stained and lacking in well defined chromatin. There was a moderate increase of fibrous tissue but many areas of interstitial cells remained.

Adrenal

Average size and appearance. The cortical layers were well demarcated; in all zones the cytoplasm was

CONTROL NO. X 9. MALE. AGED 49. Arteriosclerosis

Death followed being run over by a motor lorry.

Pituitary

Average size and appearance. The vascularity of the anterior lobe appeared to be average; there was a slight increase of fibrous tissue. The eosinophils slightly exceeded the basophils and chromophobes though the latter were numerous. The cytoplasm of both eosinophils and basophils was not deeply stained and the nucleii had not stained as darkly as usual; the chromatin was also below normal. The cleft was irregular and almost obliterated; there was no colloid. The pars intermedia consisted of some irregular layers of faintly staining pink cells with dark nucleii. The posterior lobe presented the usual picture - some pink masses and slight deposits of pigment.

Thyroid

Average size and appearance; rather a mottled surface. On section the vesicles were seen to be filled (in some cases distended) with pale pink colloid. The lining cells tended to be flattened and the nucleii indifferently stained and lacking in well defined chromatin. There was a moderate increase of fibrous tissue but many areas of intervesicular cells remained.

Adrenals

Average size and appearance. The cortical layers were well demarcated; in all zones the cytoplasm was

quite well stained and showed considerable vacuolation; the nucleii stood out clearly and were well stained; the chromatin content was satisfactory. The vascularity was average. The medullary cells were normal but there seemed to be some reduction in the amount of medulla seen.

Testes

Average size and appearance; consistency firm. The tubules were well formed and the component cells had stained well; the nucleii were rich in chromatin. There was active mitosis proceeding in the spermatocytes. The sperm heads were well stained. The intertubular connective showed no increase and the interstitial cells were normal; the cytoplasm stained well and the chromatin content was up to standard.

CONTROL NO. X 7. FEMALE. AGED 12

Apparently a mentally normal girl. She was knocked down by a motor van and received severe injuries from which she died almost instantaneously.

Pituitary Wt. .35gm.

Size average for age; normal appearance. In the anterior lobe the vascularity appeared to be average or slightly increased; the connective tissue was normal in amount and distribution. The eosinophil cells predominated; a few basophils were seen and a moderate number of chromophobes. The eosinophils showed a tendency to form acini; the cytoplasm was not very deeply stained and the nuclei varied - some being fairly deeply stained and rich in chromatin while others were pale and lacking in chromatic substance. The cleft was patent but contained no colloid. The pars intermedia consisted of clear well-formed cells whose cytoplasm was faintly granular and stained feebly with eosin; the nuclei were well stained; no acini were seen. The posterior lobe showed occasional pale nuclear structures; some pink masses of colloid (less than usually seen in adult glands). There was no pigment.

Thyroid Wt. 5.4gms.

Average size for the age; pale and of homogeneous appearance. The vesicles were seen to be full of pink colloid; no blue colloid was seen. The intervesicular

connective tissue was fine and wavey; many groups of cells with deeply staining nuclei were noticed lying between the vesicles. The cells lining the vesicles were cubical and well stained.

CONTROL NO.X 26. MALE. AGED 13.

Cause of death --- Cerebral abscess following measles.

Pituitary Wt. .5gm.

Average size for age; anterior lobe pale; obvious colloid in cleft. On section the cells of the anterior lobe were seen to be loosely arranged; all the usual cell types were well represented but the chromophobe type appeared to predominate. The eosinophils were numerous and exceeded the number of basophils. The chromophobes were scattered throughout the lobe; their nucleii were well seen and the chromatin was well marked; most of the nucleii showed one or two well marked nucleoli. The eosinophils were small and scattered; the cytoplasm of these cells was finely granular and not deeply stained; there was no vacuolation; the nucleii varied from the small dark type to the larger and pale variety (chromophobe type). The basophils appeared to be confined to the central portion of the lobe, extending backwards to the cleft; their cytoplasm was deeply but irregularly stained; the nucleii were seen with difficulty but appeared to have a rich chromatin network. The cleft was patent and contained some broken up colloid (a good deal appeared to have been lost in the preparation of the slide - this not infrequently happens). The pars intermedia was well marked; the cytoplasm of the cells was stained faintly

pink and the nucleii were small and dark with occasional large pale ones; many acini were present - these enclosed pale pink colloid. The posterior lobe presented the usual picture; there was no pigment; occasional pink hyaline bodies were present.

Pineal

Rather large and pale. The cut surface showed a few small granules of a hard gritty substance. On section there were seen to be many large pale nucleii (similar to the chromophobes in the pituitary) lying in a syncytial mass of pink staining cytoplasm; the cells were not clearly demarcated; the nucleii though pale showed a good chromatin pattern. The general vascularity was poor. In parts the characteristic wavy appearance of this organ was well seen. Practically no hyaline masses were visible, the neural portion appeared normal.

Thyroid

Rather dark in colour and of homogeneous appearance. On section there appeared to be less vesicles than usual and more intervestibular tissue. The vesicles were irregular in size and contained a variable amount of pink colloid. The cells and nucleii stained well and the whole gland seemed to be in a highly active state. The vascularity was rich and the fibrous tissue minimal.

Adrenals

R Rather small and thin; firm. On section the three zones were seen to be clearly demarcated; the cytoplasm was stained pink throughout; the staining was not deep. Throughout there was considerable vacuolation. The nucleii were not deeply stained but the chromatin was rich and the nucleoli prominent. The vascularity was rich throughout. The medulla seemed rather wasted though the portions seen were well stained.

Testes

Small and compact; the structure was firm and pale. On section the tubules were seen to be closely packed together and these were regular in size and shape. The cells and nucleii were well stained and the spermatocytes showed active mitotic division of the nucleii; there were no formed spermatozoa. The inter-tubular connective tissue was plentiful and contained many well formed interstitial cells; the nucleii of these contained a rich chromatin network. The vascular supply was rich.

CONTROL NO. X 15. FEMALE. AGED 33.

Street accident. Cause of death -- fractured skull.

Married. The uterus was reported normal.

Pituitary Wt. .65gm.

Average size and appearance; the anterior lobe was large and looked pale. On section the cell types were seen to be nearly equally represented though there was a slight preponderance of basophils and chromophobes over eosinophils. There was no increase of fibrous tissue; the vascularity appeared to be average. The basophil cells were somewhat smaller than usual and the staining was irregular; the nucleii were small and dark and were rich in chromatin. The chromophobes were numerous and their nucleii varied in size; the chromatin content was good. The eosinophils were relatively reduced in numbers; the cytoplasm was rather ragged and unevenly stained; the nucleii stood out well and contained rich chromatin. There were occasional collections of basophil colloid scattered throughout the anterior lobe. The cleft was almost obliterated but contained some scattered pink colloid. The pars intermedia was of average size and was composed of faintly staining pink cytoplasm with small dark nucleii and a few chromophobe cells. The posterior lobe was scanty; no pigment was seen; there were the usual isolated collections of pink hyaline matter.

Thyroid

Pale and homogeneous appearance. On section the vesicles were less numerous than usual and the inter-vesicular tissue was increased in amount. The vesicles contained a variable amount of pink colloid. There was a slight increase of fibrous tissue. The vascularity appeared to be normal. All the nuclei possessed good chromatin.

Adrenals

Average size and appearance. There was good demarcation between the cortex and medulla and between the cortical layers. The cytoplasm of the cortex was well stained with eosin and there was the usual degree of vacuolation. The nuclei were well stained and contained rich chromatin. The vascularity was average and there was no increase of fibrous tissue. The medulla appeared normal.

Ovaries

Both showed moderate sized cysts scattered throughout their substance; these contained jelly like substance. One large central cyst in the right ovary contained a laminated lining and some pigment; this was obviously a corpus luteum. On section this structure revealed the typical structure of a corpus luteum with the usual large pigmented luteal cells. The germinal epithelium was intact; there were a fair number of ripening Graafian follicles.

CONTROL NO. X 12. MALE. AGED 10.

Street accident. Almost instantaneous death.

Pituitary

S Small but proportional to size of body. In the anterior lobe the cells were more scattered than in the average adult gland. The eosinophil cells occupied most of the field. The eosinophil cytoplasm was irregular and diffusely stained and looked thin. The nucleii were irregular in shape but stained well and possessed rich chromatin; the nucleii were large in proportion to the amount of cytoplasm. Practically no basophil cells were seen and these were very immature in size and staining. There were several chromophobe cells; their nucleii were large and pale. The vascularity was not excessive and the fibrous tissue minimal. The cleft was rather wide and contained one large mass of pink colloid. The pars intermedia consisted of a double layer of cells whose cytoplasm stained faintly pink; the nucleii were small but deeply stained. The posterior lobe contained a number of chromophobe like nucleii and some pink masses; there was no pigment.

Thyroid

Small and pale. The vesicles were small and filled with pink colloid which showed some vacuolation; the lining cells were cubical and the nucleii well stained and rich in chromatin. The intervesicular connective

tissue was normal and there was no secondary fibrous tissue. There was plenty of intervesicular tissue with large well stained nuclei. The vascularity appeared poor.

Adrenals

Firm and pale. In the cortex the layers were not well demarcated. The cytoplasm was diffusely stained with eosin; there was no vacuolation. The nuclei stained well and possessed rich chromatin. The medulla was normal.

CASE NO. 6 151. FEMALE. AGE 34 SINGLE. OCC. NID
1st ATTACK

Cause of death --- Epilepsy

Mental State

Epileptic. Depressed and strange in manner. She had a delusion that people had been throwing stones at her; she obviously heard imaginary voices; these sometimes were very loud and unpleasant. She was fairly

CASES OF EPILEPSY

CASE PROTOCOLS AND

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Physical State

She remained fairly healthy during her period in hospital. After 4 years she developed a swollen and inflamed leg and seven days later died.

Post-mortem

Myocardial degeneration with fatty change, slight cerebral softening abscess on right leg.

Body wt.	62.5 lbs. (on admission)
Brain "	1420 gm. 62.10 lbs.
Liver "	1100 "
Pituitary	.52 "
Thyroid	.15 "

Pituitary

Average size and appearance. The vascularity seemed within normal limits; there was however a marked increase of fibrous tissue, especially marked in the centre of the lobe. The basophils and chromo-

CASE NO. C 141. FEMALE. AGED 34. SINGLE. OCC. NIL
1st ATTACK

Cause of death --- Epilepsy

Mental State

Epileptic. Depressed and strange in manner. She had a delusion that people had been throwing stones at her; she obviously heard imaginary voices; these sometimes told her that she was pregnant. She was faulty in her habits; at times was violent and resistive; for periods she would refuse food. She had frequent and severe fits, and gradually demented while in hospital.

Physical State

No gross physical lesion was discovered on admission. She remained fairly healthy during her period in hospital. After 4 years she developed a swollen and inflamed leg and seven days later died.

Post-mortem

Myocardial degeneration with fatty change, slight central softening abscess on right leg.

Body wt.	6st.2 lbs.	(on admission
Brain "	1420gms.	6st.10 lbs.)
Liver "	1100 "	
Pituitary	.62 "	
Thyroid	15 "	

Pituitary

Average size and appearance. The vascularity seemed within normal limits; there was however a marked increase of fibrous tissue, especially marked in the centre of the lobe. The basophils and chromo-

phobes were in excess of the eosinophils; the latter were markedly reduced in number. The nucleii of the chromophobes was poorly stained; in the basophils and eosinophils the nuclear chromatin was fairly well marked. The cleft was irregular and only patent in parts; there was some scattered colloid - blue and pink. The pars intermedia, which was eosinophil and chromophobe, was extensive and invaded the posterior lobe at certain points. The posterior lobe presented the usual appearance; there was some pigment and the usual pink hyaline bodies were scattered throughout the lobe.

Thyroid

This gland was of average size and appearance; there appeared to be a good deal of colloid showing in the cut surface. The gland was not sectioned.

CASE NO. C 39. FEMALE. AGED 44. MARRIED. OCC.
HOUSEWIFE.

Cause of death --- Pulmonary T.B.

Mental State

Epilepsy. Fairly frequent fits. Typical epileptic mental make-up. Gradually deteriorated and dementia set in.

Physical State

There was nothing definite to note on admission. Ten years after admission she first showed definite signs of pulmonary T.B. One year later she died.

Post-mortem.

Extensive T.B. of both lungs with cavitation and caseation. The myocardium was flabby and fatty. Most of the organs showed some degree of cloudy swelling. There was nothing specially pathological in the brain.

Body wt.	6st. 5 lbs. (average 5½st.)
Brain "	1250gms.
Liver "	1150 "
Pituitary wt.	.95 gm.

Pituitary

Rather larger than normal. The cleft contained considerable colloid. Throughout the anterior lobe there was a marked increase of fibrous tissue. The vascularity appeared to be average. There was a large cyst-like space in the anterior part of the lobe; this apparently had contained eosinophil colloid but this was lost during preparation of the section. The

basophils and eosinophils appeared to be about equally distributed. The basophils stained deeply and the nuclei were also well stained and contained rich chromatin. The eosinophils were granular and well stained; the nuclei varied, some were large and pale and eccentric, while others were small and darkly stained. The chromophobes were reduced in number but appeared otherwise normal. The cleft was wide and as above stated contained considerable colloid; most of this was lost from the section during preparation but what remained was pink. The pars intermedia was well marked; the cells stained well with the acid stain and there was a marked tendency to the formation of acini. The posterior lobe looked very pink; there were some pink hyaline masses but no pigment was seen.

CASE NO. C 42. MALE. AGED 62. OCC. BUILDERS
LABOURER

Cause of death --- Epilepsy; myocardial
degeneration

Mental State

Epilepsy. Dull and confused on admission. He had delusions of persecution and thought that people worked on him with electricity, etc. He had period of excitement; frequent fits, occurred usually at night.

Physical State

There was nothing special noted as to the physical state of this patient. He was found dead in bed one night nine years after admission.

Post-mortem

The heart was very flabby and there was marked fatty infiltration and degeneration; the left central was dilated. Scattered atheroma of aorta.

Body	wt.	lost.
Brain	"	1450gms.
Liver	"	1550 "

Pituitary

Average size. In the anterior lobe the eosinophils predominated over the basophils. The cytoplasm of the eosinophils was very granular and well stained; the nuclei were well stained and showed rich chromatin. The basophils were quite numerous and well stained. The chromophobes appeared to be reduced but were otherwise normal.

There was a marked increase of fibrous tissue throughout. The vascularity was average or slightly increased. The cleft was obliterated and contained no colloid. The pars intermedia was fairly well marked and the cells took the acid stain. The posterior lobe appeared normal.

Physical State

In addition the pupils were dilated to size of 4 mm. and 5 mm. and were slightly irregular. The general health was fairly good. The skin was frequent and there was no other abnormality. The patient was a female of 30 years of age. The patient was a female of 30 years of age. The patient was a female of 30 years of age.

Post-mortem

The patient was a female of 30 years of age. The patient was a female of 30 years of age. The patient was a female of 30 years of age. The patient was a female of 30 years of age. The patient was a female of 30 years of age.

Brain	100 g.	100 g.	100 g.	100 g.
Heart	100 g.	100 g.	100 g.	100 g.
Lungs	100 g.	100 g.	100 g.	100 g.
Spleen	100 g.	100 g.	100 g.	100 g.
Thyroid	100 g.	100 g.	100 g.	100 g.
Adrenals	100 g.	100 g.	100 g.	100 g.
Testes	100 g.	100 g.	100 g.	100 g.

CASE NO. D 84. MALE. AGED 19. SINGLE. OCC. NIL.

Cause of death --- Status epilepticus

Mental State

An epileptic having frequent and moderately severe fits. He was emotional and had outbursts of violence at times. On admission he was disorientated. His habits were at times faulty and he had a habit of exposing himself; he frequently masturbated.

Physical State

On admission the pupils were sluggish in their reaction to light and there was some slight nystagmus. No other neurological disturbances were noted. His general health remained fairly good. The fits were frequent and severe and on some occasions he passed into a condition of status epilepticus. Three years after admission he died in status epilepticus.

Post-mortem

Well nourished. Some thickening of mitral valve. Consolidation of base of left lung. Kidneys congested. Pachymeningitis haemorrhagico externa; injection of pia; cerebral softening.

Brain	wt.	1390gms.	Body wt.	10st.
Liver	"	1490 "		(average the same)
Spleen	"	230 "	Body ht.	5ft.7ins.
Pituitary	"	.5gm.	Arm length	22ins.
Thyroid	"	20 "s.	Leg "	36 "
Adrenals	"	10 "	Skull wt.	630gms.
Testes	"	45 "	" capacity	900ccs.
			" circum.	22½ins.

Pituitary

In the anterior lobe the eosinophils predominated over the basophils. The chromophobes were markedly reduced in numbers. The eosinophil cytoplasm was poorly stained and less granular than usual; the nucleii were small and deeply stained. The basophil cells were arranged chiefly round the periphery; the cytoplasm was deeply stained and the nucleii seen with difficulty. The vascularity was average and there was only a slight increase of fibrous tissue. The cleft was fairly well marked and contained some pink colloid; there were many basophil cells adjoining the cleft. The pars intermedia was very fibrous and broken up; it was composed mostly of small basophils which were deeply stained. The posterior lobe appeared rather broken up; there were many basophil cells (probably from the pars intermedia) some pink hyaline bodies; no pigment seen.

Thyroid

This gland was of average size and shape; no cystic areas were seen. On section the vesicles were seen to be irregular in size and shape; they contained pale pink colloid but were not full. The lining cells were pale and the nucleii did not stain well. The vascularity seemed increased and there was some increase of fibrous tissue.

Adrenals

Thin, soft and wasted. In all three zones the cytoplasm was broken up and stained poorly. There was an extreme degree of disintegration of the cells; the nucleii however stained well and appeared for the most part to be intact. The medulla was scanty and undergoing post-mortem changes.

Testes

These were large and firm. The tunica was somewhat thickened. The vesicles were well formed and appeared active though no spermatozoa were seen. The interstitial cells were numerous and stained well; the nucleii were dark and showed good chromatin.

CASE NO.C 191. MALE. AGED 17. SINGLE. OCC.NIL

Patient was the second child of a family of two. Epileptic fits started at the age of 14; they were mostly at night and were followed by stupor.

Cause of Death --- Epilepsy

Mental State

On admission he was restless and confused; he refused food and made many attempts to escape; his habits were faulty. Prior to admission he was of a cheerful and excitable disposition. The history states that one brother and one cousin were epileptic.

Physical State

On admission there was nothing of special note. The knee jerks were brisk. Three months after admission he died after a series of rather severe fits.

Post-mortem

The lungs appeared partially collapsed but were otherwise normal. The heart was small but the musculature fairly good. There was slight, fine atheroma of the aorta. The C.S.F. was increased but the brain was normal apart from some slight congestion.

Brain	wt.	1520gms.	Body	wt.	7st. (average
Liver	"	1130 "			7st.12 lbs.)
Spleen	"	120 "	Body ht.		5ft.11ins.
Pituitary	"	.5 "	Arm length		22 $\frac{1}{2}$ ins.
Thyroid	"	14 "	Leg	"	33 "
Adrenals	"	10 "	Skull wt.		420gms.
Testes	"	21 "	"	capacity	870ccs.
			"	circum.	21ins.

Pituitary

The anterior lobe was composed chiefly of chromo-

phobes; next in frequency were the eosinophil cells which were more numerous than the basophils. The eosinophils presented their usual appearance and stained well but had pale nucleii. The basophil cells stained fairly well but their nucleii were less deeply stained than usual. There was nothing special to note about the chromophobes. The cleft was wide and contained abundant colloid - both blue and pink. The posterior lobe showed no departure from the normal; there was no pigment. The pars intermedia was quite well marked and was chiefly eosinophil with some chromophobes cells; there was a good deal of eosinophil colloid.

Thyroid

Rather a small gland. The vesicles contained a good deal of blue colloid but they were not distended and there was no flattening of the lining cells; there was some vacuolation of the colloid. The nucleii were well stained and the chromatin well marked.

Adrenals

The glands were of usual size and appearance; the medulla appeared wasted (P.M. change?) On section the cortical cytoplasm was seen to be stained faintly pink with a good deal of vacuolation. The nucleii took the stain well and showed good chromatin. Little medulla was seen on the section.

Testes

Rather small; symmetrical; firm; the right testis was congested. Section showed diminution in the size of the tubules with lack of depth of staining of the nuclei and little chromatin. There was no evidence of spermatogenesis. The interstitial cells were fairly numerous but were not stained well; the chromatin however appeared to be fairly good. There appeared to be some increase of fibrous tissue between the tubules.

CASE NO. D 106 MALE. AGED 24. OCC. LABOURER

Cause of death --- Status Epilepticus

Mental State

History of fits since the age of 16. These usually preceded by an abdominal or cephalic aura. On admission this patient was confused and incoherent. Throughout his stay in hospital he was childish. His memory was defective and his power of attention and concentration were badly interfered with.

Physical State

There was nothing clinically abnormal reported on admission. He had repeated fits - about an average of 12 in the month. He finally went into a status epilepticus and died two years after admission.

Post-mortem

The ventricles of the brain were dilated and the c.s.f. increased. The endocardium and aorta were injected; the liver and kidneys congested.

Brain	wt.	1260gms.	Body wt.	8st.12 lbs.
Liver	"	1400 "		(average 9st.8 lbs)
Spleen	"	100 "		
Pituitary	"	.65 "		
Thyroid	"	25.8 "		
Adrenal (one)		4.4 "		
Testes		37.8		

Pituitary

In the anterior lobe there was a marked increase of fibrous tissue. The eosinophil cells predominated; the cytoplasm was well stained and the nuclei were rich in chromatin. The basophils were numerous and had deeply

staining nucleii. The chromophobes were relatively scanty; they had little chromatin. The pars intermedia was thin and poorly marked; the cells were mostly chromophobe in type. The posterior lobe was large and contained numerous cells. There was a good deal of brownish pigment.

Thyroid

The vesicles were filled but not distended with colloid - some staining pink and some a faint blue. There was a normal amount of fibrous tissue.

Adrenals

The zona glomerulosa appeared diminished in depth. The cytoplasm was pink throughout and the nucleii though irregular in size and shape stained well and showed good chromatin. The vascularity seemed to be increased. The nucleii varied greatly - some being rich in chromatin while others were very pale.

Testes

Average size. The tubules were well formed and appeared healthy and active; mitosis was seen in the spermatocytes and active spermatozoa were present. The interstitial cells were numerous, the cytoplasm staining pink and the nucleii dark with rich chromatin.

CASE NO. D 66. MALE. AGED 43. SINGLE. OCC. NIL.

1st ATTACK

No family history of insanity admitted.

Cause of death --- Pulmonary tuberculosis

Mental State

On admission there was a history of fits extending over many years; they had apparently started soon after puberty. The patient was definitely of the feeble-minded type and was unable to state the number of pennies in 2/6. He was quarrelsome and at times violent.

Physical State

Nothing very definite was noted on admission. In 1929, 4 years after admission, he showed signs of involvement of the lungs and was notified as T.B. Three years later he died. He continued to have occasional fits up to the time of death.

Body	wt. 6st.10lbs.	(average 9st.4lbs.)
Brain	" 1040gms.	Body ht. 5ft.7ins.
Liver	" 1020 "	Arm length 22 "
Spleen	" 120 "	Leg " 35 "
Pituitary	" .45 "	Skull wt. 440gms.
Thyroid	" 23 "	" capacity 870ccs.
Pineal	" .15 "	" circum. 20ins.
Adrenals	" 8 "	Aorta " 44mm.
		(Slight atheroma)

Post-mortem

showed extensive T.B. in both lungs; heart showed brown atrophy. The Pia mater was thickened and slightly opaque.

Pituitary

The anterior lobe showed a marked increase of

fibrous tissue. Chromophobe cells were numerous but the nuclei poorly stained and deficient in chromatin. The eosinophil cells were in excess of the basophils. The eosinophils tended to form acini and their cytoplasm was vacuolated. The basophils were irregularly stained; the nuclei had average chromatin and a well marked nucleolus. The cleft was poorly formed (almost closed up); there was an absence of colloid. The pars intermedia was well marked and was made up of eosinophil cells which tended to be arranged in acinar formation. There were large scattered areas of pink staining hyalin substance. The posterior lobe was more vascular than usual; many small round nuclei like bodies were seen throughout. There was a moderate amount of brownish green pigment.

Thyroid

No macroscopic abnormality. Not sectioned.

Adrenal

There was a marked fibrosis throughout. The cortex was greatly diminished and all three zones were reduced in depth. The cytoplasm was stained faintly pink and there was no vacuolation. The nuclei stood out clearly but the chromatin was reduced in amount. The medulla was reduced in amount though the cells stained well.

Testes

Small and shrunken. Marked increase of fibrous

tissue. The tubules were small and irregular and showed a general atrophy. There was no evidence of spermatogenesis. The interstitial tissue was increased in amount but the cells stained very feebly and there was a great reduction of chromatin.

CASE NO.D 28. MALE. AGED 23. SINGLE. OCC.NIL

Cause of Death --- Epilepsy; pneumonia.

Mental State

Patient was a generally feebly minded epileptic. He suffered from auditory hallucinations and at times became severely confused. Periods of impulsiveness were common. He had frequent and severe fits and died in status epilepticus a year after admission.

Physical State

No gross physical lesion found. he remained in fairly good health while in hospital.

Post-mortem

Heart normal. There was commencing consolidation at the L. apex. Brain normal.

Brain	wt.	1430gms.	Body	wt.	9 st.
Liver	"	1490 "	"	ht.	5 ft.6 ins.
Spleen	"	130 "	Arm length		22 ins.
Pituitary	"	.65 "	Leg	"	34 "
Thyroid	"	14 "	Skull wt.		500 gms.
Adrenals	"	18 "	" capacity		850 cms.
Testes	"	30 "	" circum		21½ ins.
			Aorta	"	41mm.
					(Fine atheroma)

Pituitary

Average size and naked eye appearance. In the anterior lobe the vascularity appeared to be average or slightly diminished. The lobe was highly cellular with a slight reduction of the chromophobes and increase of basophils and eosinophils; the basophils were slightly more numerous than the eosinophils. The basophils were well stained and very crowded together with an

attempt to form acini in places; there was no obvious vacuolation. The eosinophils stained well and showed coarse granulation of the cytoplasm; their nuclei were rather pale and appeared not to have much chromatin; there was, however, a well marked nucleolus in most cases. The chromophobes as above stated were reduced in number but of usual appearance. The cleft was patent and dilated; it contained a large amount of pink colloid; this was broken up. The pars intermedia was irregular in shape and broken up by increase of fibrous tissue; the eosinophil cytoplasm contained well stained nuclei; several chromophobe cells were seen but no basophils. The posterior lobe had the usual appearance; vascularity poor; a few deposits of brownish pigment and occasional pink hyaline matter.

Thyroid

Average size and appearance; homogeneous structure to the naked eye. On section the vesicles were seen to be filled but not distended with colloid (some was pink, some grey blue). The lining cells tended to be flattened and their nuclei were irregular and very pale with little nuclear structure (practically no chromatin substance showing). There was a general increase of fibrous tissue with a marked reduction of the intertubular substance. The vascularity was average or diminished.

Adrenals

Rather large and pale. The cortex appeared to be somewhat hypertrophied while the medulla appeared reduced and wasted. The cortical cytoplasm was well stained and showed a good deal of vacuolation; the nucleii stained fairly well though many were pale; the chromatin was well marked. The zona glomerulosa was decreased in depth while the zona reticularis appeared deeper than usual. The vascularity was above the average and there was an increase in the number of capillary sinuses and these were packed with blood corpuscles. The medulla was wasted and seemed to have undergone some P.M. change.

Testes

Average size or slightly larger; firm. The tubules appeared well formed; the cytoplasm was well stained as were the nucleii; the chromatin was rich; there was active mitosis in the spermatocytes; spermatogenesis was present. The interstitial cells were numerous but poorly stained and the chromatin was deficient.

CASE NO.D 16. FEMALE. AGED 15.

There was Mentally deficient from birth.

1st Cause of death --- Broncho-pneumonia

Mental State

1st Patient was an under-developed girl who had been completely retarded in mental growth since birth - congenital idiocy. No She had suffered from fits from an early age. She was unable to talk or answer questions. She was restless and noisy at times and faulty in habits. She appeared to have no mind. She had frequent fits.

Physical State

2nd Nothing special to note except the general under-development; did not menstruate. There was unfortunately no history as to any previous menstruation.

Post-mortem

3rd Broncho-pneumonia; heart normal; gall-stones; appendix thick and congested.

Body wt. (average)	6st.11lb.	Body ht.	5ft.2ins.
Brain	wt. 1150 gms.	Arm length	19ins.
Liver	" 1250 "	Leg	" 31½ "
Pituitary	" .55 "	Skull wt.	560gms.
Spleen	" 265 "	" capacity	800ccs.
Thyroid	" 18 "	" circum.	21ins.
Adrenals	" 10.2 "	Aorta	" 40mm.
			(No atheroma)

Pituitary

4th In the anterior lobe the basophil cells predominated over the other types, the cytoplasm stained deeply and the chromatin was plentiful. The eosinophil cells were scanty but were deeply stained; there was a marked re-

duction.in the usual number of chromophobe cells.

There was some increase of fibrous tissue; the vascularity was average. The capsule showed some thickening.

Thyroid

A symmetrical gland showing no macroscopic departure from normal. Not sectioned.

Adrenals

Average naked eye appearance. On section the zona glomerulosa showed a basophil cytoplasm with deeply staining nucleii. The zona fasciculata cytoplasm was eosinophil and vacuolated; the nucleii in this area appeared dark in some cells and large and pale in others. In the zona reticularis the cytoplasm was basophil and vacuolated and the nucleii were variable as in the middle zona. The medulla was well marked and contained cyst like areas containing pink hyaline matter (amorphous).

Ovaries

Both ovaries were markedly cystic; the right contained a small superficial cyst while the left contained a large cyst occupying an area nearly five times the actual size of the ovary; this contained a clear fluid. On section the Graafian follicles were seen to be undeveloped and contained only one layer of cells; the ova were pale and structureless. The germinal epithelium appeared normal. There were areas of old corpora lutea but no recent luteal tissue was seen.

Pineal

The confluent cytoplasm was basophil in staining reaction. The nuclei stained feebly and resembled the chromophobe nuclei of the pituitary.

CASE NO.C 225. MALE. AGED 24. FORMER OCCUPATION:
LABOURER.

Fits started at 24 years of age.

Father died at 56 from cancer. Mother died of paralysis (?). One brother suffered from epilepsy.

Cause of death --- Status Epilepticus

Mental State

On admission was strange in manner and suffered from visual hallucinations. He had a delusion that people wanted to kill him. He had frequent fits and these were usually preceded by an aura which took the form of a ringing in the ears, this occurred about five minutes before the fit started.

Physical State

Nothing of special interest was noted in this case history on admission. Later the pulse showed some irregularity probably due to extra systoles. Fits were frequent. In one months he had no fewer than 110 fits. Finally he went into a typical status epilepticus and died of exhaustion.

Post-mortem

Some thickening of mitral valve. Lungs oedematous; brain appeared normal; slightly injected.

Body wt.	averaged 9st.5lbs.	Body ht.	5ft.8ins.
Brain	wt. 1400 gms.	Arm length	22 ins.
Liver	" 1390 "	Leg	" 32 "
Spleen	" 135 "	Skull wt.	390gms.
Pituitary	" .9 "	" capacity	730ccs.
Thyroid	" 37 "	" circum.	22ins.
Adrenals	" 14 "	Aorta	" 6lmm.
Testes	" 28 "		
Pineal	" .4 "		(No atheroma)

Pituitary

In the anterior lobe there was a marked increase of fibrous tissue; the vascularity appeared to be increased. The chromophobe cells showed an absolute increase above the other two types; the eosinophils and basophils showed an equal distribution. The chromophobes presented the usual picture though the nucleii stained feebly and did not show much chromatin. The eosinophils occurred mostly at the periphery and showed a good deal of vacuolation of their cytoplasm. The basophils were increased towards the pars intermedia; the cytoplasm tended to be vacuolated. The pars intermedia was well marked and made up chiefly of darkly staining eosinophil cells and well stained nucleii; there was a good deal of colloid present in the cleft which was patent. The posterior lobe showed infiltration with the cells of the pars intermedia; there was no pigment; hyaline pink bodies were present.

Thyroid

Large and symmetrical; dark and congested; the vesicles were full but not distended with pale blue colloid; the secreting cells well stained and the nucleii mostly small and dark but there were a variable number which were large and pale.

Adrenals

Of good size and firm to the touch. The cyto-

plasm was mostly eosinophil and fairly well stained; there was considerable vacuolation; the nucleii were paler than usual and there was some irregularity in their outline; the chromatin was not perceptibly diminished. The zona reticularis showed an increase of fibrous tissue; the cytoplasm was of a brownish colour and the cell nucleii were pale and showed no nuclear structure. The medulla was well marked; there was considerable elastic tissue present.

Testes

Symmetrical and firm. There was considerable increase of fibrous tissue between the tubules which presented a broken up appearance. There was a reduction in the number of cells normally present and there was no sign of any spermatogenic activity. The interstitial cells were also greatly reduced in number; they were very irregular in shape and did not stain well.

Pineal

There was a large amount of scattered basophil colloid. The cytoplasm was irregular and stained pink and blue; the nucleii were pale.

CASE NO. D 90. FEMALE. AGED 42 YEARS. MARRIED (5 CHILDREN)

HOUSEWIFE.

Cause of Death --- Lobar Pneumonia

Mental State

The history stated that patient had had fits since the age of 18. On admission she was confused and disorientated. There was a considerable degree of feeble-mindedness. At times she was excited. She had during her time in hospital many and severe fits. There was some evidence of auditory hallucinations. She died seven years after admission from lobar pneumonia.

Physical State

There was no note of any clinical abnormality on admission and she remained in fair health until she contracted pneumonia and died.

Post-mortem

The lungs were congested and consolidated. Kidneys congested. The brain was congested otherwise average in appearance.

Brain wt.	1350gms.	Body wt.	8st.5lbs.
Liver wt.	1490 "	" ht.	
Spleen wt.	220 "	Arm length	20ins.
Pituitary wt.	.7 "	Leg "	31 "
Thyroid wt.	23 "	Skull wt.	
Adrenals wt.	10 "	" capacity	840ccs.
Ovaries wt.	14 "	" circum.	21ins.
Pineal wt.	.25 "	Aorta "	51mm.
		(no atheroma)	

Pituitary

The eosinophils and basophils appeared to be present in the eosinophilic substance. No germinal layer was seen: there

in nearly equal numbers. The chromophobes were reduced. There was some increase in fibrous tissue and the vascularity was average. The chromophobes were of the usual type and appeared to be normal. The basophils showed vacuolation and a paleness of their cytoplasm. The eosinophils presented a normal picture and their nuclei stained well (they were mostly eccentric). The cleft was irregular and not well marked; there was practically no colloid. The pars intermedia was irregular and composed of all three cell types of which the chromophobes predominated. There was nothing special to note about the posterior lobe.

Thyroid

This gland was firm and rather dark in colour and showed no cysts. On section the vesicles were seen to be full but not distended with pink colloid. The cells stained well but showed poorly staining nuclei with deficient chromatin. There was remarkably little fibrosis.

Adrenals

Both were thin and showed wasting of the medulla. The cytoplasm of the cortex was eosinophil and vacuolated; the nuclei were scanty and were poorly stained throughout with a few exceptions.

Ovaries

Each ovary contained a large cyst (about half the size of the organ) and these contained a grey jelly like substance. No germinal layer was seen; there

were many scars of old corpora lutea. There were no Graafian follicles and no recent corpora lutea. The epithelial cells were devoid of chromatin.

Pineal

This organ was highly cellular. The cells were mostly collected into groups which were separated from each other by masses of fibrous tissue. The cytoplasm was pink and the nuclei stained well and showed good chromatin. There were no calcareous deposits and little neuroglial tissue was seen. The vascularity was poor; there were some masses of pink colloid scattered throughout.

ALL THE MENTAL SYMPTOMS
usually found in G.I.s. She was confused and
CASES OF GENERAL
paralyzed, and had no insight into her condition.
PARALYSIS OF THE
arms and legs at times. Her habits were
INSANE

CASE PROTOCOLS AND

PATHOLOGICAL DESCRIPTIONS

is positive.

CASE NO. D. 71. FEMALE. AGED 35 YEARS. MARRIED. NO
CHILDREN. 1st ATTACK. HOUSEWIFE.

There was a history of mental trouble in the family;
nature not recorded.

Cause of Death --- General Paralysis of the Insane.

Mental State

Patient had, on admission, all the mental characteristics usually found in G.P.I. She was confused and disorientated; she had no insight into her condition. She was emotional and noisy at times. Her habits were faulty.

Physical State

The pupils were unequal and failed to react to light. The knee jerks were exaggerated and there were tremors of the tongue and hands. The Wassermann reaction was strongly positive.

During the year she was in hospital, before her death, she had occasional attacks of pyrexia without obvious demonstrable cause; occasionally she had seizures.

Post-mortem

showed the typical signs of G.P.I.

Body wt.	5st.10lbs.	(average 7st.12lbs.)	
Liver wt.	1070gms.	Body ht.	5ft.4 $\frac{1}{2}$ ins.
Brain "	1080gms.	Arm length	19 $\frac{1}{2}$ ins.
Spleen "	50gms.	Leg "	34ins.
Pituitary wt.	.85gms.	Skull wt.	730gms.
Thyroid wt.	23gms.	" capacity	800ccs.
Pineal wt.	.3gm.	" circum.	21ins.
Adrenals wt.	21gms.	Aorta circum.	48mm.
Ovaries wt.	5gms	(Slight atheroma)	

Pituitary

The dural capsule surrounding the gland was thickened. Throughout the anterior lobe there was an increase of fibrous tissue. Chromophobes predominated; the nucleii of these cells were large and pale and possessed little chromatin. The eosinophils were numerous and exceeded the basophils. The eosinophil cytoplasm was paler than usual and was not vacuolated; the nucleii were pale but the chromatin was well marked. The basophil cells were reduced and the cytoplasm vacuolated and not stained well. The cleft was well marked and contained a good deal of both eosinophil and basophil colloid. The pars intermedia was rather broken up and composed chiefly of eosinophil cells. The posterior lobe shows an infiltration with chromophobe cells and a fair amount of eosinophil matter.

Thyroid

Macroscopic appearance average; no cysts seen. On section there appeared to be a marked reduction of the secreting cells and a striking increase of fibrous tissue. The vesicles were distended with basophil colloid.

Adrenals

Both glands were considerably larger than normal and the cortex was definitely hypertrophied on both sides; the medulla was well defined. All three zones seemed deeper than usual. The cytoplasm was stained

irregularly, some parts being more deeply stained than adjacent areas; the nucleii also varied and it was noted that the depth of the staining of the nucleii varied proportionately with that of the cytoplasm; dark nucleii being found in well stained cytoplasm. The nucleoli were strikingly obvious in many nucleii. There was a good deal of vacuolation of the cytoplasm in all areas. The vascularity was above the average and many of the bloodvessels seemed to contain a pink staining colloid substance (secretion). The medulla was rather broken up and contained several masses of pink amorphous matter.

Ovaries.

Small and fibrous. No Graafian follicles seen. No corpora lutea present though many scars of old ones seen. The germinal layer was intact. The blood vessels were numerous and showed considerable thickening of the walls.

CASE D. 64. MALE AGED 66 YEARS. SINGLE. R.C.PRIEST.

1st ATTACK.

Cause of Death --- General Paralysis of the Insane.

Mental State

On admission was confused and disorientated. He appeared to be completely lost to his surroundings. He was restless and noisy at times. The general mental state was that of G.P.I. During the five months he was in hospital he went slowly downhill and died in a wasted condition.

Physical State

The pupils were unequal and failed to react to light. There was a right internal strabismus. The knee jerks were slightly exaggerated and there was some tremor of the tongue. The Wassermann reaction was strongly positive.

Post-mortem

showed the typical signs of G.P.I. and a terminal bronchitis.

Body wt.	9st.12lbs. (average 11st.)		
Brain wt.	1470gms.	Body ht.	5ft.9ins.
Liver "	1450 "	Arm length	22ins.
Spleen wt.	120 "	Leg "	37ins.
Pituitary wt.	.7 "	Skull wt.	420gms.
Thyroid wt.	24 "	" capacity	950ccs.
Pineal wt.	.25 "	" circum.	22ins.
Adrenals wt.	14 "	Aorta circum.	63mms.
Testes wt	47 "	(marked atheroma)	

Pituitary

The posterior lobe was relatively large. In the anterior lobe there was a marked increase of fibrous

tissue both fine and coarse. The basophils predominated and were arranged in acini; these cells were very deeply stained and the nucleii could not be seen. The chromophobes were numerous. There were practically no eosinophils. There was a good deal of basophil matter scattered throughout the lobe. The cleft was irregular and practically obliterated; there was scanty basophil colloid. The pars intermedia was fairly well marked and was composed of basophil and chromophobe cells. The posterior lobe was cellular; several basophil cells being seen and a fair amount of basophil colloid. There was no pigment. The pars tuberalis contained well marked eosinophil cells and some of the colloid had found its way into the posterior lobe (this was the only obvious source for the pink colloid seen in the lobe).

Thyroid

This gland was not symmetrical; it was of a darkish colour and presented a slightly cystic appearance to the naked eye. On section the vesicles were seen to be filled with pale pink colloid. The lining cells were only slightly flattened. The nucleii were well stained for the most part though there were some which stained very poorly and were obviously deficient in chromatin.

Adrenals

These glands were large and nearly symmetrical. The medulla was wasted. The cytoplasm throughout was

faintly pink and showed a moderate amount of vacuolation. The nucleii were rather pale and deficient in chromatin. There was an increase of fibrous tissue.

Testes.

Large and symmetrical. The epithelium of the tubules was well stained and the nucleii stood out well and showed mitosis; there was evidence of spermatogenesis. The interstitial tissue was well marked and many cell groups showed good chromatin in the nucleii while some were pale and lacking in chromatin. There was a fair amount of brownish pigment.

Pineal

The usual picture of pale pink cytoplasm presenting a syncytial appearance and nucleii of a chromophobe type. There was a quantity of pale pink colloid. Some calcareous patches.

CASE NO. C. 206. MALE AGED 36 YEARS. SINGLE. 1st ATTACK

TAILOR

Cause of Death --- G.P.I.

Mental State

On admission was restless and confused; his habits were faulty and he was resistive to attention. He was transferred to this hospital from Pentonville prison to which place he had been confined on a charge of theft.

Physical State

The blood and c.s.f Wassermann reactions were strongly positive. The pupils were slightly unequal and failed to react to light. He became rapidly and progressively weaker and died within a month of admission.

Post-mortem

brain atrophy; fatty change; lungs congested; liver fatty; brain-pia thickened, opaque and adherent; granulations in the 4th ventricle; ventricle dilated; C.S.F. increased.

Brain wt.	1190gms.	Body wt.	7st.
Liver wt.	1550 "	" ht.	5ft.7ins.
Spleen wt.	80 "	Arm length	20 $\frac{1}{2}$ ins.
Pituitary wt.	.8 "	Leg "	33 $\frac{1}{2}$ "
Thyroid wt.	16 "	Skull wt.	540gms.
Adrenals wt.	17 "	" capacity	830ccs.
Testes wt	8 "	" circum.	21ins.
		Aorta "	51mm.
		(slight atheroma)	

Pituitary

Average size. In the anterior lobe the vascularity was average and there was no increase of fibrous tissue.

The eosinophil cells predominated; these stained well and showed the usual two types of nuclei (small and dark and large and pale; the latter with little chromatin, the former showing good chromatin). The basophils were relatively few in number but stained well. The chromophobes were present in large numbers and had their usual appearance. The pars intermedia was well marked and consisted of much pink cytoplasm with dark well staining nuclei. The cleft was well marked and contained a good deal of blue and pink colloid. The posterior lobe contained some scattered pigment; otherwise usual appearance.

Thyroid

Average size and appearance; almost symmetrical; no cystic areas seen. On section the vesicles were seen to contain much pale blue colloid; this showed slight vacuolation; the nuclei were well stained. Fibrous tissue average.

Adrenals

Rather above the average size; the cortex was relatively enlarged while the medulla was rather wasted. The cortical cytoplasm was pink and granular but showed practically no vacuolation; the nuclei showed variable staining - some being pale while others were dark; many showed distinct nucleoli. The medulla was very wasted and appeared to have undergone post-mortem change.

Testes

These were very small and rather soft; they were rather dark and mottled. The vascularity was increased and the tubules were very atrophied and irregular. No spermatozoa seen; the nuclei stained fairly well and the chromatin appeared rich. The interstitial cells were poorly stained and were irregular and small; there was an increase of pigment; the nuclear chromatin was reduced.

CASE NO. 11. FEMALE AGED 32 YEARS. TRAINING (1.07.11)

1st ATTACK AT AGE OF 3-4.

Cause of Death -- Pulmonary Tuberculosis

Mental State

Dull and generally apathetic; disinterested and introverted; violent and impulsive at times. No auditory hallucinations; faulty habits. No improvement during two years in hospital.

Physical State

CASES OF SCHIZOPHRENIA

There were occasional attacks of morbidly melancholia.

CASE PROTOCOLS AND

The patient was rather singular in their reaction. After

PATHOLOGICAL DESCRIPTIONS

a few years she commenced to lose weight; there was cough and signs of involvement of the lungs. There was considerable

involvement of the bowels. Ten years after she died

in a very emaciated state.

Post-mortem

showed extensive pulmonary T.B. with cavitation and cavitation; there was ulceration of the small intestine;

the brain appeared normal; the liver was enlarged.

Brain wt.	1150gms.	Body wt.	55.5 lbs. (at death)
Liver wt.	1375 "	" ht.	5ft. 3ins.
Spleen wt.	95 "	Arm length	24ins.
Pituitary wt.	.8 "	Leg "	24ins.
Thyroid wt.	19 "	Skull wt.	1450gms.
Adrenals wt.	12 "	" capacity	250cc.
		" circumference	24ins.
		Abdomen	49ins.

Pituitary

Average size and appearance. In the case of 11.

CASE NO. D. 11. FEMALE AGED 52 YEARS. MARRIED (1 CHILD)
1st ATTACK AT AGE OF 3-6.

Cause of Death --- Pulmonary Tuberculosis

Mental State

Dull and generally apathetic; disinterested and introverted; violent and impulsive at times. Auditory hallucinations; faulty habits. No improvement during ten years in hospital.

Physical State

On admission there were no signs of organic disease. There were occasional attacks of megrainous headache. The pupils were rather sluggish in their reaction. After a few years she commenced to lose weight; there was cough and signs of involvement of the lungs. There was considerable looseness of the bowels. Ten years after she died in a very emaciated state.

Post-mortem

showed extensive pulmonary T.B. with caseation and cavitation; there was ulceration of the small intestine; the brain appeared normal; the liver was amyloid.

Brain wt.	1160gms.	Body wt.	6st.5lbs. (at death)
Liver wt.	1370 "	" ht.	5ft.3ins.
Spleen wt.	90 "	Arm length	20ins.
Pituitary wt.	.8 "	Leg "	32ins.
Thyroid wt.	19 "	Skull wt.	440gms.
Adrenals wt.	12 "	" capacity	830ccs.
		" circum.	21ins.
		Aorta "	49mm.

Pituitary

Average size and appearance. In the anterior lobe

the basophils predominated; these cells were arranged in acini; the cytoplasm was deeply stained and granular; there was some vacuolation; the nucleii were dark and appeared to have rich chromatin. The eosinophils were numerous; their cytoplasm was granular and well stained; there was considerable vacuolation; the nucleii varied; some were very poorly stained; many masses of pink cytoplasm appeared to be without any nucleus. The chromophobes were average in appearance but seemed to be slightly reduced in numbers; the nucleii showed fairly good chromatin. The general vascularity appeared to be average and there was no obvious increase in fibrous tissue. The cleft was irregular and contained some broken up pink colloid. The pars intermedia was not extensive; the cells were eosinophil and chromophobe; the nucleii stained well. The posterior lobe was rather broken up; there was no pigment to be seen.

Thyroid

Average size; appeared cystic and contained a good deal of colloid. Not sectioned.

Adrenals

Large and asymmetrical. There seemed to be some general cortical hypertrophy; the cytoplasm in all layers stained pink; in the zona fasciculata the cytoplasm was granular and not vacuolated. The nucleii were well stained throughout and there was no deficiency in chroma-

tin. The vascularity seemed average; There was no increase of fibrous tissue. The medulla appeared normal.

CASE NO. C 220. FEMALE AGED 50 YEARS. MARRIED (NO CHILDREN)

1st ATTACK

Cause of Death --- Pulmonary Tuberculosis

Mental State

On admission she was noisy and emotional; childish in her manner; there were auditory hallucinations. Occasionally she was faulty in her habits. She was destructive and very restless. There was little material change in her condition while she was in hospital.

Physical State

On admission she was rather thin but no demonstrable organic lesion was found. About a year after admission she developed a cough and irregular pyrexia and started to lose weight; there were some signs of involvement of both lungs and she was diagnosed T.B. and sent to the sanatorium. Four years after admission she died.

Post-mortem

Extensive miliary T.B., broncho-pneumonia at left base; brown atrophy of heart muscle; aorta slight atheroma.

Brain wt.	1300gms.	Body wt.	6 st. (at death)
Liver wt.	875 "	" ht.	5ft.3ins.
Spleen wt.	95 "	Arm length	20ins.
Pituitary wt.	.75 "	Leg "	28ins.
Thyroid wt.	17 "	Skull wt.	320gms.
Adrenals wt.		" capacity	690ccs.
		" circum.	19½ins.

Pituitary

Average size and appearance. The anterior lobe had an average vascularity and there was a slight general

increase of fibrous tissue with many fibroblasts. The chromophobe type of cells predominated. The basophils and eosinophils appeared to be present in about equal numbers. The chromophobes possessed the usual large nucleus which in most cases showed a well marked nucleolus; the chromatin was scanty. The basophils were deeply stained and showed marked vacuolation; the nucleii were not clearly seen. Eosinophils were coarsely granular and vacuolated; the nucleii were usually eccentric but in many cases there were masses of pink cytoplasm without any nucleus. The cleft was patent and contained a little colloid (staining both eosinophil and basophil). The pars intermedia was poorly marked. The posterior lobe showed no departure from the usual picture.

Thyroid

Average size. Asymmetrical; pale and mostly homogeneous. The vesicles were seen to be distended with colloid most of which was blue in colour but in some areas it was stained pink. The lining cells were flattened. The nucleii were pale and deficient in chromatin. There was a marked increase of fibrous tissue which was destroying the gland tissue. In another section it was seen that the same conditions held good but there was more pink colloid.

Adrenals

Asymmetrical and large. There were extensive areas

of haemorrhage into both glands; these seemed particularly extensive in both cortical areas. On section there was little cortical substance left and what was seen was very distorted. The remaining portions of the medulla appeared fairly normal.

CASE NO. C.156. FEMALE. AGED 50 YEARS. SINGLE. DOMESTIC
SERVANT

Cause of Death --- Cerebral haemorrhage

Mental State

Admitted in 1908 and was then childish and silly; untidy. At times she became noisy and excited. During her long time in hospital she gradually demented becoming more and more feeble-minded.

Physical State

No gross physical lesion was found on admission nor until just before death. She was always obese and the general metabolic level was lowered; she was noted to have an enlarged thyroid but was never given any thyroid medication.

23 years after admission she developed signs of having had a cerebral haemorrhage:- loss of consciousness with stertorous breathing; pupils small and failed to react to light; before losing consciousness she complained of pain in the back of the head. There developed a divergent squint and the planter response was extensor.

Died the next day.

Post-mortem

Heart showed some brown atrophy; lungs congested; haemorrhage into L. cerebellar hemisphere. Slight atheroma of aorta.

Body wt.	12 st.	Skull wt.	640gms.
" ht.	4ft. 11ins.	" capacity	900ccs.
Brain wt.	1250gms.	" circum.	21ins.
Liver wt.	1590 "	Arm length	19ins.
Spleen wt.	170 "	Leg "	30 $\frac{1}{2}$ ins.
Pituitary wt.	.7 "		
Thyroid wt.	63 "		

Pituitary

Average size. In the anterior lobe there was a marked increase of fibrous tissue and great reduction of the number of cells visible; the vascularity appeared to be diminished. Chromophobes predominated; practically no eosinophils seen; several basophils. The chromophobes had large nucleii which were pale and very deficient in chromatin; the basophils were very broken up and showed much vacuolation; their nucleii stained fairly well but showed great reduction of chromatin. The cleft was distended with a large mass of pale blue colloid; this was broken up and interposed throughout the mass were several smaller masses of pink colloid. The pars intermedia was very broken up and all that was seen was a disintegrated mass of poorly staining cells with very pale nucleii. The posterior lobe appeared normal.

Thyroid

Exceptionally large; the cut surface was brown in colour and several cysts were scattered throughout. On section it was seen that the vesicles were filled but not distended with colloid; most of this was pink but there were areas in which it was blue. The cells were mostly cylindrical and the nucleii had stained well and possessed good chromatin.

CASE NO. C 73. FEMALE AGED 25 YEARS. SINGLE. SHOP
ASSISTANT. 1st ATTACK.

Cause of Death --- Disseminated Sclerosis Endocarditis.

Mental State

On admission she was emotional and childish; she was restless and at times noisy; her habits were faulty. There was little change in her mental state while in hospital.

Physical State

On admission she had signs of Disseminated Sclerosis; there was marked motor impariment; the speech was slurred; the planter responses were extensor on both sides; both knee jerks were exaggerated. The abdominal reflex was absent. There was some wasting of the arms and legs. The pupils reacted normally but there was lateral nystagmus of both eyes.

Colloidal gold curve 21111100000

Wassermann negative.

Cells and globulin within normal limits.

Patient died within two months of admission.

Post-mortem

Marked fatty degeneration of the heart; sub-scute endocarditis; aortic and mitral pulmonary congestion and oedema; kidneys congested. Patches of sclerosis throughout the central nervous system.

Body wt. 7st.8lbs.

Brain wt. 1250gms.

Pituitary Wt. .6gm.

Average in size and appearance. In the anterior lobe the vascularity was average; there was a marked increase of fibrous tissue both generalised and in localised patches. The basophils were markedly increased; their cytoplasm was well but not deeply stained; there was no vacuolation; the nucleii were small, dark and round. The eosinophils were fairly numerous but irregular and the cytoplasm was not as granular as usual; there was no vacuolation; the nucleii were poorly stained. The chromophobes were reduced in number; throughout the lobe there were occasional masses of basophil colloid. The cleft was irregular and contained broken up masses of colloid - some blue, others pink. The pars intermedia was very irregular and all three cell types were represented; there was a great deal of fibrous tissue. The posterior lobe presented the usual picture; there were the customary masses of pink hyaline substance; no pigment was seen.

CASE NO. D 114. MALE AGED 36 YEARS. SINGLE. Occ. NIL.

Cause of Death --- Pulmonary Tuberculosis (Miliary)

Mental State

On admission was depressed and generally dull. There was a good deal of confusion and some disorientation. He was restless and resistive to attention. The habits were faulty. There was little change in the mental state before death which occurred a month after admission.

Physical State

On admission there was dullness and crepitations at the right apex and the sputum contained T.B. There was a bilateral ptosis; both pupils were equal and reacted to light and accommodation. There was a progressive decline and patient died just under a month after admission.

Post-mortem

Both lungs showed extensive miliary T.B. There were enlarged and calcified mesenteric glands. The heart muscle was fairly good and there was no valvular lesion. Slight fine atheroma of the aorta.

Brain wt.	1550gms.	Body wt.	6st.13lbs.
Liver wt.	1000 "	" ht.	5ft.7ins.
Spleen wt.	70 "	Arm length	22ins.
Pituitary wt.	.7 "	Leg "	35 "
Thyroid wt.	30 "	Skull wt.	620gms.
Adrenals wt.	11 "	" capacity	840ccs.
Testes wt.	26 "	" circum.	22 $\frac{1}{2}$ ins.

Pituitary

The vascularity of the anterior lobe was average. There was one area of fibrosis otherwise the fibrous tissue

was not increased. The basophils predominated over the eosinophils; the chromophobes were numerous and probably exceeded the basophils. The basophilic cytoplasm was not deeply stained and the nucleii were clearly seen - they contained well staining chromatin. The chromophobes contained for the most part nucleii of the large type. The eosinophils were well stained; The cytoplasm was granular and no vacuolation was seen. The nucleii varied in the usual manner - some being small and dark, others being large and pale. The cleft was prominent and contained one mass of basophil colloid. The pars intermedia was well marked and the cells eosinophil with well stained nucleii. The posterior lobe showed no departure from the usual picture; there was no pigment seen.

Thyroid

The vesicles were full but not distended with colloid, some of which was blue and some pink. The lining cells showed some flattening but the nucleii were well stained and possessed rich chromatin. The fibrous tissue was not increased and the vascularity was average.

Adrenals

These were of average size, appearance and consistency. The cytoplasm of the cortex stained pink and showed the usual vacuolation; the nucleii were deeply stained and appeared to contain plenty of chromatin. The cytoplasm of the zona fasciculata showed the greatest amount of

vacuolation. The medulla was very wasted. This may have been due to P.M. change.

Testes

Slightly below average size. The tubules appeared normal though no formed spermatozoa were seen. The spermatocytes showed active mitosis and the nuclei were deeply stained. The interstitial cells were fairly numerous but were not well stained; there was a good deal of pigmentation.

General State

There was some emaciation at the time of death. There was no gross evidence of disease. After admission to the hospital the patient was kept in bed and died on the 12th day in hospital.

Post-mortem

Body was well developed and appeared healthy. There was no gross evidence of disease. The organs were normal in size and position.

Brain	130g	100g
Liver	120g	100g
Spleen	100g	100g
Stomach	100g	100g
Intestine	100g	100g
Heart	100g	100g
Lungs	100g	100g
Kidney	100g	100g
Testis	100g	100g
Pituitary	100g	100g

Histology

In the testis the tubules were normal in size and structure. The interstitial cells were fairly numerous but were not well stained; there was a good deal of pigmentation.

CASE D 40. MALE. AGED 23. SINGLE. OCC.RESEARCH
STUDENT

Cause of death --- Acute bronchitis

Mental State

On admission this patient was extremely restless and resistive to all attention. He was agitated in manner and very confused, being unable to give any account of himself; there was evidence of auditory and visual hallucinations. A diagnosis of acute dementia praecox was made.

Physical State

There was some emaciation and the tongue was furred. There was no gross clinical lesion to be noted. Shortly after admission he developed an acute attack of bronchitis and died on his tenth day in hospital.

Post-mortem

Brain: pia thickened and injected. Heart normal; aorta showed some fine atheroma; muco-pus in both lungs.

Body	wt.	7st.4lbs.	Arm length	22ins.
"	ht.	5ft.8ins.	Leg "	36 "
Brain	wt.	1390gms.	Trunk "	
Liver	"	1200 "	Skull wt.	420gms.
Spleen	"	130 "	" capacity	210ccs.
Pituitary	"	.7 "	" circum	81ins.
Thyroid	"	20 "	Aorta "	41ins.
Adrenals	"	10.3 "		
Testes	"	30 "		
Pineal				

Pituitary

In the anterior lobe the chromophobes predominated while the eosinophils exceeded the basophils. The

chromatin of the nucleii in all three types of cell stained well and did not appear deficient. The basophils were scanty and the cells poorly formed. The vascularity was average and there was only a slight increase of fibrous tissue. The cleft was prominent but devoid of colloid. The pars intermedia showed abundant eosinophil cells with well stained nucleii. The posterior lobe showed inclusions of eosinophil and basophil cells; there was no increase of pigment.

Thyroid

Asymmetrical but of average appearance. The vesicles were filled but not distended with colloid staining pale blue. There was an excess of fibrous tissue and a diminution in the number of cells; the cell nucleii did not stain as deeply as usual.

Adrenals

The right gland was small and wasted. The left showed some thickening of the capsule; the layers showed the usual distribution; there was a moderate amount of vacuolation. The cell nucleii stained well and the chromatin was well seen. The medulla had undergone P.M. changes.

Testes

Symmetrical and firm and of a yellowish colour. The tubules appeared normal and there was evidence of spermatogenesis. The interstitial cells were scanty and irregular in shape; the nuclear chromatin was deficient.

Pineal

Highly cellular - the cytoplasm of some cells was eosinophil while others are basophil; there were some collections of colloid substance.

Physical State

CASE NO.D 96. MALE. AGED 18. SINGLE. OCC.CLERK.
1st ATTACK.

Cause of death --- Acute Meningitis (Parotid
Abscess)

Mental State

On admission was in a state of semi-stupor alternating with periods of excitement. He was destructive and generally restless. He was markedly impulsive, and was disorientated and was incoherent in his speech. His habits were faulty; there was some evidence of auditory hallucinations.

Physical State

He was extremely difficult to examine on admission but there did not appear to be any gross lesion. Three days after admission it was noticed that the left parotid was swollen; this was incised. There was some fever. The following day the patient died.

Post-mortem

showed an acute meningitis; an otitis media and a deep-seated parotid abscess.

Brain	wt.	1370gms.	Body wt.	?
Liver	"	1370 "	" ht.	5ft.6ins.
Spleen	"	120 "	Arm length	20ins.
Pituitary	"	.65 "	Leg "	34 "
Thyroid	"	34 "	Skull wt.	440gms.
Adrenals	"	9 "	" capacity	920ccs.
Testes	"	16 "	" circum.	21ins.
Pineal	"	.15 "	Aorta circum.	38mm.
			(Fine atheroma)	

Pituitary

The eosinophils were reduced and were exceeded by both the basophils and the chromophobes. The vascu-

larity was average and there was no increase of fibrous tissue. Chromophobes were of the usual type and showed no abnormality. The basophils stained well and had good nucleiii with well marked chromatin. The easinophils stained poorly and the nucleii showed little chromatin. The cleft was well marked but contained no colloid. The pars intermedia was composed of chromophobe cells and extended backwards into the posterior lobe; there were a few easinophils and basophils. The posterior lobe was more cellular than usual and showed many spindle shaped cells. There was a large amount of brownish pigment and in many parts there was pink hyaline substance.

Thyroid

This organ presented a darkish and congested appearance. On section it was seen that the vesicles were full and in some cases distended with blue colloid. The lining cells tended to be flattened. The nucleii were well stained and possessed good chromatin. There was a slight amount of fibrosis.

Adrenals

These were below the average size and both the cortex and the medulla were reduced. The cytoplasm was pink and granulated and showed moderate vacuolation. the nucleii stained well and possessed fairly rich chromatin. There was an increase of fibrous tissue throughout the gland.

Testes

These were very undersized. The tubules were small and irregular and under-developed. All the cells were small and poorly stained and the nuclei were very deficient in chromatin; there was no mitosis and no spermatozoa were seen. The interstitial cells were large and fairly numerous but they were pale and the nuclei were badly stained and deficient in chromatin.

CASE NO.D 70. MALE. AGED 25. OCC. CLERK (SHIPPING).

1st ATTACK.

Cause of death --- Acute delirious mania.

Mental State

On admission he was depressed and confused. There was marked disorientation and lack of appreciation of his position and surroundings. He was obviously hearing imaginary voices and suffering from visual hallucinations. There were many fleeting delusions; i.e. that he was being gassed, etc. At times he had violent emotional outbursts; he was difficult with his food and his habits were faulty.

Physical State

There were no signs of organic disease on admission. He became progressively weaker although still showing no physical signs. He died 15 days after admission. The urine on admission showed a trace of albumen; many uric acid crystals and acetone. The Wassermann reaction was negative.

Post-mortem

revealed little of interest; there was some injection of the trachea and stomach; faecal accumulation and slight injection of the pia mater.

Brain	wt.	1390gms.	Body wt.	9st.1lb.
Liver	"	1350 "	" ht.	5ft.8ins.
Spleen	"	170 "	Arm length	22ins.
Pituitary	"	.7 "	Leg "	37ins.
Thyroid	"	41 "	Skull wt.	350gms.
Adrenals	"	10 "	" capacity	910ccs.
Testes	"	24 "	" circum.	21½ins.
			Aorta "	57mm.

Pituitary

In the anterior lobe the basophil cells predominated to a remarkable extent; next in frequency were the chromophobes. The eosinophils were markedly reduced. Two types of basophils were noted; one type being much paler than the other; the type with the pale cytoplasm contained pale nucleus. The eosinophils were poorly stained and less granular than usual; there was some vacuolation. In all types of cells the chromatin was reduced in the nuclei. The vascularity was average and there was no obvious increase of fibrous tissue.

The cleft was well marked but devoid of colloid. The pars intermedia was well marked and consisted of three or four layers of cells which were mostly eosinophile but several chromophobes were seen. The posterior lobe was very dense; the fibrils were increased but the cells diminished. Many collections of pink hyaline matter were seen. A few collections of basophil substance were seen.

Thyroid

Usual appearance to the naked eye; large and homogeneous; one cyst was seen. On section the vesicles were seen to be filled but not distended with pale pink colloid. The lining cells were not flattened; they stained quite well and showed good chromatin. There was a moderate increase of fibrous tissue.

Adrenals

These glands showed some wasting of the medulla but the cortex was large and well marked. Throughout the cortex the cytoplasm was well stained; there was a good deal of vacuolation and the nucleii stood out well. Some of the cells were breaking up and the cell contents lying free; these showed excess of pigment. The medulla was wasted and showed an increase of fibrous tissue.

Testes

These were firm to the touch but were below the predicted size. The tubules were small and the cell pattern irregular. There was no evidence of spermatogenesis. The interstitial cells were numerous but the cytoplasm was irregular and the nucleii poorly stained and deficient in chromatin.

CASE NO.D 87. MALE. AGED 18. SINGLE. OCC. SHOP
ASSISTANT. 1st ATTACK.

No family history obtained.

Cause of death --- Acute delirious Mania.

Mental State

On admission he was confused and restless. There was evidence of auditory and visual hallucinations. He was resistive and refused food. There was marked constipation and the skin was dull in colour.

Physical State

There were no signs of organic disease on admission. His general state was poor and he looked toxic. Three weeks after admission he developed an abscess on the left arm and this resulted in a spreading cellulitis of the arm and a few days later he died.

Post-mortem

Body well nourished. Endocardium injected. Lungs oedematous and congested - some pleurisy (old). Brain appeared normal. Aorta showed fine atheroma.

Brain	wt.	1610gms.	Body wt.	Not taken.
Liver	"	1670 "		
Spleen	"	190 "		
Pituitary	"	.75 "		
Thyroid	"	14 "		
Adrenal (one)	"	4.4 "		
Testes	"	29 "		

Pituitary

In the anterior lobe there appeared to be a reduction in the number of cells seen. The basophils slightly predominated but all types were well represented. The

vascularity was increased. There was some increase of fibrous tissue and the cells tended to be arranged in acini. The basophil cells were more granular than usual and were irregularly stained; the nuclei appeared rather pale and the chromatin was slightly deficient. The eosinophils stained poorly and the nuclei were deficient in chromatin; several masses of pink cytoplasm were seen without visible nuclei. The chromophobes were numerous and were mostly of the large type; the chromatin being poorly marked. The cleft was well marked and contained masses of pink colloid which presented a honeycombed appearance and contained several eosinophil cells. The pars intermedia was well marked and very cellular, being composed of numerous eosinophil cells with much pink colloid passing into the cleft. The posterior lobe showed an increased vascularity and many pink hyaline masses.

Thyroid

The vesicles appeared less numerous than usual but the cells were plentiful. There was a fair amount of pink colloid filling but not distending the vesicles. There was a slight increase of fibrous tissue; the vascularity appeared average; the chromatin in the nuclei appeared normal in amount.

Adrenal

There seemed to be a slight increase in the size of the cortex with a proportional diminution of the medulla.

The cytoplasm stained irregularly and was very vacuolated. The sinus spaces contained pink masses (secretion?). The medulla was scanty and wasted (P.M. change).

Testes

These were of average size or slightly reduced. The tubules were irregular in size and showed little lumen. The cells stained well and active mitosis was seen. The interstitial cells were reduced in number and the chromatin seemed deficient. The general vascularity was increased and the blood vessels were packed with corpuscles.

CASE NO.D 173. MALE. AGED 30. SHOW CARD MAKER.

1st ATTACK.

One uncle insane(?)

Cause of death --- Acute bronchitis

Mental State

Prior to admission there was a history of having been psycho-analysed. On admission he was restless, destructive and incoherent. His habits were faulty. There was well marked negativism and general resistiveness. He was completely disorientated and lacked all insight into his condition. There were auditory hallucinations. At times he was emotional and abusive. His condition did not change much during his short time in hospital.

Physical State

There were practically no signs of organic disease on admission. The Wassermann reaction was negative. The urinary findings unimportant with the exception of greatly increased excretion of phosphates. Five months after admission he started to lose weight despite the fact that he was eating well; no evidence of organic disease. Six months after admission he died after a few days pyrexia with cough.

Post-mortem

showed an acute bronchitis with muco-pus in both lungs but without consolidation.

Brain	wt.	1470gms.	Body wt.	6st.6lbs.
Liver	"	1270 "		(average 8st.)
Spleen	"	80 "	Body ht.	5ft.7ins.
Pituitary	"	.9 "	Arm length	21ins.
Thyroid	"	11 "	Leg "	35 "
Adrenals	"	11 "	Trunk "	26½ "
Testes	"	32 "	Skull wt.	420gms.
Heart	"	200 "	" capacity	900ccs.
			" circum.	21½ ins.
			Aorta "	47 mm.
				(Fine atheroma)

Pituitary

In the anterior lobe there was a remarkable absence of basophil cells. The whole section was stained pink from the excessive number of eosinophils. The chromophobes were also present in great numbers. The eosinophil cytoplasm was rather ragged and the cell margins were difficult to demarcate; the cells at the periphery were stained well and here the cells were arranged in acini. The nucleii were large and pale and the chromatin deficient. The chromophobes showed the usual picture. There was a moderate increase of fibrous tissue and the vascularity was average. The cleft was very wide and was filled with colloid (only a little remained in the section and this was pink. The pars intermedia was thin and rather scanty; it consisted of pink cytoplasm with large, fairly dark nucleii which were however deficient in chromatin; there was considerable fibrous tissue on both sides of the secreting cells. The posterior lobe had the usual appearance; there was no pigment; pink hyaline bodies were fairly numerous.

Pineal

Large and active; in appearance it was pale and soft. On section there was seen to be much pink cytoplasm without distinct cell demarcation. The cytoplasm was granular but no vacuolation was noticed. The nucleii were large and dark and rich in chromatin. No calcareous areas were seen; there were several small masses of pink hyaline substance and these were best seen scattered throughout the neuroglial part; in this part there were several round pale collections of some amorphous substance.

Thyroid

Small; symmetrical and pale; no cysts visible. On section the whole gland looked disorganised. The vesicles were irregular and the cells were considerably altered in shape. There was a great deal of very pink colloid which in some cases filled the vesicles and in other parts was scanty; there was some vacuolation of the colloid. The cell nucleii stained very poorly and little nuclear structure was seen; there was a marked reduction of chromatin. There was a general increase of fibrous tissue; the vascularity was average.

Adrenals

Both glands were firm; the cortex was pale and thin; the medulla dark and well marked. The zona fasciculata and glomerulosa had pink staining cytoplasm which showed extensive vacuolation and the typical

'empty' appearance. The nucleii in these zones were of two types:

- (1) Medium sized staining pink and of very irregular structure; the nuclear structure here was poor and the chromatin practically absent.
- (2) A more regular nucleus with two or three nucleoli but deficient in chromatin.

The cells of the zona reticularis showed pink granular cytoplasm which was not vacuolated; these cells had the same two types of nucleii; the better stained ones predominating. The general vascularity was diminished. The medulla was quite well marked and appeared normal.

Testes

The testes were unequal, the right being appreciably larger than the left; they were pale and rather more soft than usual. The tubules were irregular in structure and incomplete in their conformation. The cells were unequal and the nucleii varied in size, shape and staining reaction. No spermatozoa were seen. There was a marked reduction of the inter-tubular connective tissue. The interstitial cells were numerous but the cytoplasm was stained unevenly and the nucleii although stained fairly well were deficient in chromatin.

Pancreas

The cells of this gland stained well and the nucleii showed a good distribution of chromatin. The Islet cells of Langerhans appeared normal - both the Alpha and Beta cells being clearly seen.

NOTE: The distribution of hair on this patient was of some interest; hair was profuse on trunk and legs; there was a moderate growth on the forearms. On the face and pubes it was normal.

CASE NO.D 77. MALE. AGED 25. SINGLE. 1st ATTACK.

Cause of Death --- Bulmonary tuberculosis.

Mental State

On admission he was depressed and introverted, with suicidal tendencies. Auditory hallucinations were also present; bizarre delusions; e.g. that he had snakes inside him. He was difficult with his food. His habits were usually clean. Throughout his time in hospital he was actively suicidal and made repeated attempts to injure himself necessitating constant supervision.

Physical State

Soon after admission he developed phthisis; this ran a typical and rather prolonged course for some five years before he died; there were remissions but progressive weakness.

Post-mortem

showed extensive T.B. of both lungs with general wasting of the body. There was no amyloid disease. The brain was not wasted.

Brain	wt.	1370gms.	Body wt.	6st.11lbs.
Liver	"	1320 "		(average 10st.)
Spleen	"	160 "	Body ht.	5ft.9ins.
Pituitary	"	.45 "	Arm length	22ins.
Thyroid	"	13 "	Leg "	37 "
Pineal	"	.35 "	Skull wt.	480gms.
Adrenals	"	11 "	" capacity	910ccs.
Testes	"	23 "	" circum.	21ins.
			Aorta "	48mm.

Pituitary

The three cell types in the anterior lobe were about equally distributed with a slight predominance of baso-

phils. Both basophils and eosinophils showed a tendency to adopt an acinar formation. The basophils showed two types of nucleii - small and darkly staining - large and pale. There was a little vacuolation of the cytoplasm. The general chromatin is fair; it was slightly reduced but not as much as would have been expected from the mental and physical state. The eosinophil nucleii were for the most part eccentrically placed and were small and dark; as is commonly found there were several masses of cytoplasm without any apparent nucleii. The chromophobes were numerous and of the usual type. The vascularity was average; there was no increase of fibrous tissue. The cleft was small and no colloid was seen. The posterior lobe was small and nothing abnormal was noted.

Thyroid

Small, pale and homogeneous. The vesicles were distended with very pale colloid; the colour varied from a pale blue to a pale pink. The nucleii were of average size but were deficient in chromatin.

Adrenals

These were firm and pale and the cortex looked large in proportion to the medulla. The cytoplasm was generally basophil and was markedly vacuolated; the nucleii were small, round and dark; the chromatin appeared normal. The zona reticularis appeared deeper than usual and the cytoplasm was eosinophil and almost

synsyttial; there were numerous deposits of pinl colloid. The nucleii were small and dark. The medulla was scanty and seemed to have undergone post-mortem change.

Testes

Rather soft and definitely small. The tubules had a ragged appearance; no spermatozoa were seen. The interstitial cells were numerous but poorly stained; there seemed to be an increase of intertubular connective tissue.

Pineal

Very cellular; the cells tended to run together and had the appearance of a syncytium. The cytoplasm was faintly eosinophil and the nucleii showed two types: small and dark and a larger type which did not stain deeply. The neuroglial portion was reduced. The vascularity was poor; a few calcareous patches were noted before section.

CASE NO.D 76 FEMALE. AGED 28. MARRIED. 1st ATTACK.

No children and no history of any miscarriage.

No family history.

Cause of Death --- Acute Pancreatitis

Mental State

On admission she was dull and semi-stuporose.

There were auditory and visual hallucinations. Fleeting delusions occurred and she thought that people were under her bed and that her husband was in the ward. There was a marked sexual trend in the delusions. She would frequently expose herself. There was little change in the general mental state before the patient died one month after admission. She became less confused and the delusions were not so manifest, however.

Physical State

Patient was in a collapsed state on admission and there was a history of a subacute appendix. Apart from occasional slight fever and indefinite pain and tenderness in the right illiac fossa there was little to note on her physical state. Three weeks after admission she was operated on and the appendix removed; it was chronically inflamed. Four days after operation, however, she died after displaying signs of some further abdominal trouble.

Post-mortem

revealed an acute pancreatitis with marked fat necrosis; heart fatty; lungs congested; localised peritonitis over head of pancreas. Brain normal.

Body wt.	(8st.6lbs.	Body ht.	5ft.5ins.
	(girdle fat)	Arm length	21ins.
Brain wt.	1410gms.	Leg "	35ins.
Liver wt.	1330 "	Skull wt.	450gms.
Spleen "	80 "	" capacity	860ccs.
Pituitary	1 "	" circum.	21ins.
Thyroid wt.	39 "	Aorta "	42 mm.
Pineal "	.25 "	Some fine atheroma	
Adrenals "	5 "	oresent.	
Ovaries "	14 "		

Pituitary

The three cell types were equally represented. The basophils were well stained but irregularly disposed; the nucleii were small and dark and the chromatin was seen with difficulty. The chromophobes were numerous and the nucleii stood out well and possessed good chromatin. The eosinophils were well stained and showed coarsely granular cytoplasm; the nucleii varied greatly, some small and dark but the majority large and pale; some cells seemed to be devoid of nucleii. The cleft was poorly marked and empty (no colloid). The pars intermedia was poorly marked and composed of all three types of cells with chromophobes predominating. The posterior lobe was more vascular than usual but showed nothing of particular note.

Thyroid

Of homogeneous appearance; no cysts seen. The vesicles were distended with pale grey colloid and the lining cells were flattened; there was some increase of fibrous tissue.

Adrenal

Only one gland examined. It was of average size

and appearance. Throughout the three zones the cytoplasm was basophil in colour. The nucleii varied considerably; some were pale and poor in chromatin while others stained well and showed good chromatin; the pale nucleii predominated. The medulla was well marked.

Ovaries

These were of good size and firm to the touch. Graafian follicles were seen throughout the organ. There were many areas of scarring pointing to the presence of past corpora lutea; these tended to be surrounded by fibrous tissue. The general vascularity was increased. There were some recent luteal cells present (note that the patient was not menstruating while in hospital).

Pancreas

This organ was large and pale and very fatty. The portion near the head was undergoing fat necrosis. There was marked fibrosis throughout and the Islets of Langerhans were reduced and altered and the cells atrophied.

CASE NO.D 156. FEMALE. AGED 36. OCC.NURSE. SINGLE.

Cause of death --- Pulmonary tuberculosis.

Mental State

On admission she was depressed but showed a marked schizophrenic reaction. She was essentially of the 'shut in' type. There were ideas of persecution, e.g. she thought she was being accused of stealing. There were auditory hallucinations. She was destructive, tearing up her clothing. Her habits were faulty. She made no progress and became if anything worse. She was dull and lifeless but with occasional noisy outbursts.

Physical State

On admission there was a slight degree of anaemia. She menstruated regularly. Seven years after admission she was suspected of having pulmonary tuberculosis but this was not proved. Later this diagnosis was confirmed and eleven years after admission she died.

Post-mortem

showed advanced pulmonary T.B. and considerable involvement of the small intestine (scattered tubercles).

Brain	wt.	1370gms	Body wt.	7st.7lbs.
Liver	"	1830 "		(average 9st.)
Spleen	"	180 "	Body ht.	5ft.3ins.
Pituitary	"	.65 "	Arm length	21ins.
Thyroid	"	25 "	Leg "	33ins.
Adrenals	"	18 "	Skull wt.	600gms.
Ovaries	"	13 "	" capacity	900ccs.
			" circum	21½ins.
			Aorta "	
			(Slight atheroma)	

The distribution of hair was average.

Pituitary

There was an increase of fibrous tissue throughout the anterior lobe. The basophils predominated over the eosinophils. The chromophobes were numerous. The basophil cells were very feebly stained and several showed marked vacuolation. The nucleii were not deeply stained but seemed to have average chromatin. The chromophobes were average and their nucleii were pale and did not show much chromatin. The eosinophils were well stained and appeared to be collected into groups which showed an attempt to form acini. The eosinophil nucleii stained well and appeared to have a reasonable amount of chromatin. The vascularity was average. The cleft was well marked; it was devoid of colloid. The pars intermedia was ragged and consisted of a few basophil cells with dark vacuolated cytoplasm and dark nucleii. The posterior lobe showed considerable invasion with basophil material. There was a large amount of brownish green pigment.

Thyroid

Average size and appearance. Not sectioned.

Adrenals

These glands were large and the cortex was hypertrophied. The medulla was somewhat broken up in the section. The cytoplasm throughout stained faintly blue and was vacuolated. The nucleii were undergoing various stages of degeneration; many appeared only as shadows. The general vascularity was average.

Ovaries

The right ovary contained a large cyst about one third the size of the organ; this contained a jelly-like fluid which did not appear on the section. Throughout the ovary there were occasional ripening Graafian follicles. Several old luteal scars were seen but no fresh luteal tissue was noted.

CASE NO. D 23. FEMALE. AGED 48. OCC.DAILY DOMESTIC.

MARRIED. NO CHILDREN. 1st ATTACK.

Cause of death --- Morbus Cordis (Aortic and Mitral)

Mental State

On admission and during observation in hospital this patient had delusions of persecution; these were not systematised. She was confused and had hallucinations of sight and hearing. There was no improvement in her mental state during her time in hospital.

Physical State

Except for a mitral systolic murmur at the apex of the heart (which appeared to be fairly well compensated) there was nothing to note in her physical condition.

The Wassermann reaction was negative. There was a notable irregularity in the heart's action producing at times a tachycardia and at other times a pronounced bradycardia.

Post-mortem

examination showed a double valvular lesion, there being vegetations on both the mitral and aortic valves.

Body wt. averaged 7st.6lbs.	Body ht. 5ft.8ins.
Brain wt. 1280gms.	Arm length 22ins.
Liver " 1590 "	Leg " 32 "
Spleen " 220 "	Skull wt. 480gms.
Pituitary " 1.1 "	" capacity 840ccs.
Thyroid " 21 "	" circum 22½ins.
Adrenals " 15 "	Aorta circum.
Ovaries "	(Scattered atheroma)
Pineal " .2 "	

Pituitary

In the anterior lobe the chromophobe and basophil cells were far in excess of the eosinophils; the chromophobes being the most numerous. The chromophobe nuclei were rich in chromatin. The basophile cells were well stained and showed some vacuolation of their cytoplasm; there was a tendency for the cells to adopt an acinar formation. The basophil cells were reduced in number but stained well and the nuclei were prominent. The vascularity was average and there was some increase of fibrous tissue especially marked in one area. The cleft was patent but irregular; it contained some pink colloid. The pars intermedia was reduced in size and showed excessive fibrosis; the cells composing it were basophil and had dark nuclei; the cells adopted the usual acinar formation and in many cases enclosed colloid which stained pink. The posterior lobe was more cellular than usual and contained an excessive amount of greenish brown pigment; many chromophobe cells were seen but there was an absence of any colloid or hyaline matter; there were very few blood vessels.

Pineal

R rather larger than usual. The cytoplasm stained faintly pink and the nuclei were of the usual type (similar to the chromophobe nuclei of the pituitary). There occurred several masses of colloid - some pink

and others blue. There was some scattered brownish green pigment.

Adrenals

Rather larger than usual; consistency firm and colour somewhat darker than is usually found. The cytoplasm in all three zones stained well (pink) and the nucleii appeared to be rich in chromatin. There was a good deal of vacuolation of the cytoplasm. In the zona glomerulosa the cytoplasm had a broken up appearance and the nucleii were small and dark. The medulla had undergone post mortem change.

Ovaries

Both ovaries had cysts attached to them; these cysts contained clear fluid; the fluid from the cyst of the left ovary was slightly blood-stained. The right ovary was congested and showed the presence of a recent corpus luteum. The left ovary appeared normal, (apart from the large cyst). Both ovaries were deficient in Graafian follicles although the germinal epithelium appeared normal. There were several areas of extravasated blood.

CASE NO.C 204. FEMALE. AGED 34. SINGLE. OCC.
COUNTING HOUSE CLERK.

Cause of death --- Mitral disease.

Mental State

Mentally she was a typical dementia praecox. On admission she was dull and semi-stuporose; she was slightly resistive and there was some periodic flexibilitas cerea. She made little or no progress during her stay in hospital.

Physical State

There was a pronounced pre-systolic murmur at the apex of the heart - advanced mitral disease with poor compensation; her extremities were cold and blue and cyanosed. She died one year after admission.

Post-mortem

Button-hole mitral stenosis; liver, spleen and kidneys congested.

Brain	wt.	1090gms.	Body wt.	6st.11lbs.(at death)
Liver	"	1340 "	"	ht. 5ft.8ins.
Spleen	"	170 "	Arm length	21ins.
Pituitary	"	.6 "	Leg	35 "
Thyroid	"	17 "	Skull wt.	430gms.
Adrenals	"	13 "	" capacity	690ccs.
Ovaries	"	8 "	" circum.	20½ins.
			Aorta	42mms.
			(Alight atheroma)	

Pituitary

Average size and appearance. The anterior lobe showed an average vascularity and only a slight increase of fibrous tissue. The chromophobe cells predominated; the nucleii of these stained feebly and showed a reduc-

tion of chromatin. The basophils were reduced in number and were not well stained. The eosinophils were fairly numerous but the nucleii showed deficient chromatin. The cleft was patent and contained a fair amount of pink colloid. The pars intermedia was well marked and consisted of pink staining cytoplasm with well stained nucleii. The posterior lobe showed an increase of neuroglia and a considerable amount of pigment.

Thyroid

Average size and appearance. The vesicles were well filled but not distended with basophil colloid. The lining cells were not flattened. There was an increase of fibrous tissue. The cell nucleii showed no deficiency of chromatin.

Adrenals

Slightly larger than usual; firm. The cortex was poorly stained - taking the eosin faintly; there was considerable vacuolation; the nucleii varied in their power of taking the stain; some were dark while others were very pale; their chromatin content varied accordingly. There was a slight increase of fibrous tissue. The medulla was prominent and stained as usual.

Ovaries

Small and fibrous. No Graafian follicles seen; the germinal layer was poorly marked and indifferently stained. No corpora lutea were observed.

CASE NO. C 190. FEMALE AGED 50 YEARS. MARRIED (4 CHILDREN)

1st ATTACK

Cause of Death --- Acute Bronchitis

Mental State

On admission she was confused and rambling; her speech was incoherent and she was destructive in her habits. There was a good deal of restlessness and excitable periods were noted. There were auditory hallucinations. This state changed to one of depression with occasional agitation.

Physical State

Throughout her stay in hospital she was bronchitic; there was frequent cough, worse in the winter; apart from this and a slightly enlarged heart there was no sign of other organic disease. Five years after admission she developed an acute bronchitis and died.

Post-mortem

The lungs showed a slight pleurisy with much muco-pus in the smaller bronchi; the heart showed brown atrophy and fatty change. Aorta atheromatous.

Brain wt.	1210gms.	Body wt.	7st.12lbs.(average 9
Liver wt.	1270 "	" ht.	5ft.6ins.
Spleen wt.	120 "	Arm length	20ins.
Pituitary wt.	.65 "	Leg "	30ins.
Thyroid wt.	20 "	Skull wt.	500gms.
Adrenals wt.	15 "	" capacity	690ccs.
Ovaries wt.	10 "	" circum.	21ins.
Pineal wt.	.05 "		

Pituitary.

In the anterior lobe the gland substance seemed thinned. The chromophobe cells predominated. The baso-

phils were next in frequency, these were well stained with very dark nucleii; there was some vacuolation of the cytoplasm. The eosinophils appeared normal and were well stained. The vascularity was average and there was only a slight amount of fibrous tissue. The cleft was marked and contained a large amount of pink colloid. The pars intermedia was not very well marked and was made up of basophil cells. The posterior lobe was broken up and contained some brownish pigment.

Thyroid

of average size and appearance; roughly symmetrical. On section the vesicles were seen to contain blue colloid but not in sufficient quantity to cause distention. The cells and their nucleii stained well and the chromatin was average. The vascularity was average and there was no great increase of fibrous tissue.

Adrenals

The medulla was very wasted and deficient. The cortex was composed of poorly staining cytoplasm (faint pink). There was a marked vacuolation; the nucleii were irregular and some were obviously undergoing degenerative change (P.M.) The nucleii of the zona reticularis were more deeply stained; here too the cytoplasm had taken the stain better.

Ovaries

These were of average size or slightly large for the patient's age. The germinal layer was well marked. No

Graafian follicles were seen. Several areas of pink scar tissue were seen - these represented old corpora lutea; no recent luteal cells were seen. One area contained some blue colloid (?)

CASE NO. C 215. FEMALE AGED 32 YEARS. MARRIED (2 CHILDREN)

1st ATTACK

Cause of Death --- Pulmonary T.B.

Mental State

On admission she was strange in manner; introverted and obviously lost to her surroundings. She had emotional outbursts often accompanied by weeping. There was evidence of auditory hallucinations. There was little mental change to note during the time she was in hospital.

Physical State

On admission she had advanced pulmonary tuberculosis in both lungs; her condition became steadily worse despite open air treatment in the sanatorium and she died eighteen months after admission.

Post-mortem

Extensive pulmonary T.B. in both lungs; liver, kidneys and spleen showed amyloid change.

Body wt.	5st.12lbs.	Arm length	19ins.
Brain wt.	1100gms.	Leg "	30ins.
Liver wt.	1650gms.	Skull wt.	390gms.
Spleen wt.	170gms.	" capacity	740ccs.
Pituitary wt.	.65gms.	" circum.	20ins.
Thyroid wt.	13gms.	Aorta circum.	44mm.
Adrenals wt.	12gms.		
Ovaries wt.	10gms.		

Pituitary

In the anterior lobe the chromophobes were the most numerous cells seen; the basophils were very numerous and the eosinophils were scanty. There was a well marked reduction in the chromatin content of all the nuclei;

these were poorly defined and did not stain well. There was an increase in fibrous tissue throughout the gland, most marked in the anterior lobe. The vascularity of the anterior lobe appeared average. The cleft was patent and contained a moderate amount of basophil colloid. The pars intermedia showed an increased vascularity. The cells were eosinophil with a number of chromophobe cells scattered about. There was a tendency to acinar formation; the spaces containing basophil colloid. In some areas it was possible to see the basophil substance present in the blood spaces. The posterior lobe appeared normal; some eosinophil bodies were seen; the vascularity was poor.

Thyroid

Rather a small gland of usual appearance; no cysts seen. The vesicles were filled but not disrended with pale blue colloid. The cell nucleii were poorly stained and were markedly deficient in chromatin. There was an increase of fibrous tissue.

Adrenals

Of average size but rather soft texture. The capsule was somewhat thickened and the zona glomerulosa of somewhat greater than normal depth; in this layer the cells were well stained and showed good chromatin granules. In the zona fasciculata the cells stained poorly and the nucleii were deficient in chromatin. The cells of the zona

reticularis were eosinophil and showed vacuolation - the nucleii were well stained and showed fairly good chromatin. The medulla was rather deficient and had undergone post-mortem changes.

Ovaries

The ovaries were roughly equal in size. No Graafian follicles were seen in the section examined. The general vascularity of the gland was good and the vessels showed marked thickening of their walls. Many old corpora lutea were seen but no active luteal cells were visible. Many spindle cells were seen throughout the fibrous tissue.

(ONE CHILD BORN SEVERAL DAYS
 BEFORE ADMISSION)
 1-10-1934

Cause of death - Perforated Intestine

Mental State

History and resistance to all attempts

History and resistance to all attempts

MISCELLANEOUS CONDITIONS

CASE PROTOCOLS WITH

PATHOLOGICAL DESCRIPTIONS

As above stated she had been delivered of a normal

History and resistance to all attempts

Post-mortem

showed an apparently normal involuting uterus of

Body wt. not taken	Arm length	24 cm.
Brain "	Leg "	38 "
Liver "	Skull "	23 cm.
Spleen "	" "	" "
Thyroid "	" "	" "
Adrenals "	" "	" "
Pancreas "	" "	" "

CASE NO. C 221. FEMALE. AGED 41. MARRIED.

(ONE CHILD BORN SIXTEEN DAYS
BEFORE ADMISSION).

1st ATTACK.

Cause of death --- Puerperal insanity.

Mental State

Restless and resistive to all attention when admitted. At times she was noisy and talkative. Throughout she was confused and incoherent and without knowledge of time and place. She apparently suffered from visual and auditory hallucinations. Her habits were at times faulty.

Physical State

As above stated she had been delivered of a normal child without complications and after a normal pregnancy only 16 days before admission. The urine showed a bacilluria and pyuria and her general physical condition was far from good. There did not appear to be any obvious infection of the genital tract and only a slight discharge was noted and this was not offensive.

Post-mortem

showed an apparently normal involuting uterus of which the endometrium was not inflamed. There was a well marked phlegmasia alba dolens of the left leg. The other organs appeared relatively healthy.

Body wt.	not taken.	Arm length	20ins.
Brain "	1370gms.	Leg "	32½ "
Liver "	1270 "	Skull wt.	530gms.
Spleen	wt. 100 "	" capacity	1000ccs.
Pituitary	" 1 "	" circum.	21½ins.
Thyroid	" 52 "	Aorta "	41mms.
Adrenals	" 16 "	(Slight atheroma)	
Pineal	" .35 "		

Pituitary

Large and well formed. In the anterior lobe the usual cell types appeared in about equal distribution. The basophil cells had an acinar arrangement and the nucleii tended to be rather pale and the structure did not stain well. The eosinophils were coarsely granular and well stained; they too were arranged in an acini; the nucleii were well stained and, as in the basophils, the chromatin was well marked. The chromophobes were fairly numerous but did not dominate the picture; the nucleii were of two types - large and small and their distribution appeared about equal. The cleft was narrow and devoid of colloid. The pars intermedia was prominent; it appeared as masses of eosinophil cells, in some cases lying so closely together as to present the appearance of a syncytium; in others the cells were arranged in acini which contained pink colloid. The whole gland was very vascular and there was no increase of fibrous tissue.

Thyroid

The gland was large and cystic. The vesicles were distended with blue colloid; there was a good deal of fine fibrosis. The cell nucleii were well stained and showed good chromatin.

Adrenals

All zones showed considerable vacuolation. The cytoplasm was pink and the nucleii well stained and

showed a well marked nucleolus and obvious chromatin.

Ovaries

Long and narrow. There were a few Graafian follicles; no recent luteal cells were seen though there were plenty of scars of previous corpora lutea. The vascularity appeared average.

Pineal

This gland was large; there were no calcareous deposits. The cells were arranged in a syncytial manner and there was little demarcation; the nuclei were similar to those of the pituitary chromophobe type but the chromatin was scanty. The two parts of the gland were clearly demarcated and in the neuroglial part globular masses of colloid were seen - pink, blue and colourless. There was some greenish pigment scattered throughout the gland.

CASE NO.D 104. FEMALE. AGED 52. SINGLE.
DOMESTIC SERVANT.

History of some alcoholic indulgence.

Cause of death --- Cerebral tumour; glioma.

Mental State

On admission she was confused and disorientated. She was suffering from auditory hallucinations of an unpleasant type. The behaviour was emotional and there were frequent outbursts of weeping. Visual hallucinations appeared soon after admission. She was resistive and faulty in her habits and required constant care and supervision. Prior to admission there was a history of lapses of memory and her relatives stated that she seemed to have a vacant expression.

Physical State

On admission there was no sign of organic disease and examination of the C.N.S. showed nothing except a coarse tremor of the hands. The Wassermann reaction was negative and the blood count normal. Three months after admission she became comatose; the blood pressure was at this time 140/95. Slight pyrexia (101); pulse 100; resp. 28. There was some twitching of the left angle of the mouth. Some days later there was a pronounced papilloedema of both discs. The C.S.F. was under pressure but was normal in other respects. The blood N.P.N. was 40 gms. per 100 ccs. All reflexes were increased; the planter reflex was flexor. The abdominal reflex was absent. Three weeks later she died.

Post-mortem

The brain showed marked softening and gliomatous infiltration of both frontal lobes. The ventricles were dilated and the c.s.f. increased in amount. Sections of the frontal areas confirmed the tumour to be a glioma.

Brain	wt.	1400gms.	Body wt.	10st.
Liver	"	1220 "	(average 10st.10lbs.)	
Spleen	"	100 "	Body ht.	
Pituitary	"	1.4 "	Skull wt.	450gms.
Thyroid	"	10.5 "	" capacity	850ccs.
Adrenals	"	9.4 "	" circum.	21 $\frac{1}{2}$ ins.
Ovaries	"	5.5 "	Arm length	20 ins.
			Leg "	30 "

Pituitary

Large, with apparent increase in the size of the anterior lobe. There was some increase of fibrous tissue. The eosinophils and basophils appeared in roughly equal numbers; there were many chromophobes. The eosinophils were coarsely granular and the cytoplasm showed much vacuolation; the nucleii were large and pale and the chromatin was reduced. The basophils were irregularly stained and the nucleii small and dark. The chromophobes showed two types of nucleii - small, round and dark, the other type having large pale nucleii - the former were much more numerous (80%). The vascularity was average and there were areas of thrombosis. The cleft was quite well marked but devoid of colloid. The pars intermedia showed much fibrosis and the cells were mostly basophil with a number of chromophobes -

there was some basophil colloid adjoining this area. The posterior lobe appeared dense; there was a greater vascularity than usual and an excessive deposit of brownish pigment.

Thyroid

Small and of homogeneous appearance. The vesicles were filled but not distended with very pale blue colloid. There was some increase of fibrous tissue; the cells looked healthy.

Adrenals

The cytoplasm was stained faintly with the acid stain; there was considerable vacuolation but the nucleii appeared well stained and showed good chromatin. The medulla was wasted and contained some masses of pink amorphous matter.

Ovaries

Small and fibrotic; one small cyst present.

CASE NO.D 85. FEMALE. AGED 47. MARRIED.
(4 CHILDREN). 1st ATTACK.

One brother has mental trouble.

Cause of death --- Cerebral softening;
Chronic bronchitis

Mental State

On admission she was drowsy and confused. Her memory was very poor both for recent and remote events. At times she was noisy and excited and inclined to be violent. One of her chief complaints was of numbness in the hands. She did not show any improvement while in hospital.

Physical State

There were few physical signs on admission; she was badly constipated and the breath was offensive. Five months after admission she became stuporose; her pulse was weak and there was marked coldness and cyanosis of the extremities. The right side of the body showed definite weakness and there was facial asymmetry. There was a general lack of tonus on the right side of the body. She improved but remained dull and depressed. A few days later she had a seizure followed by a period of stupor which was accompanied by diarrhoea; a few days later she died.

Post-mortem

Lungs emphysematous; gall stones. Liver and spleen fibrosed. Some generalised cerebral softening.

Brain	wt.	1230gms.	Body wt.	9st.10lbs.
Liver	"	1240 "	(average 10st.)	
Spleen	"	60 "	Body ht.	5ft. 4ins.
Pituitary	"	.75 "	Arm length	20 $\frac{1}{2}$ ins.
Thyroid	"	13 "	Leg "	33 ins.
Adrenals	"	16 "	Skull wt.	450gms.
Ovaries	"	6 "	" capacity	780ccs.
			" circum.	21ins.
			Aorta "	48mm.
			(No atheroma)	

Pituitary

There was a striking reduction in the number of chromophobes. The eosinophils exceeded the basophils. The whole anterior lobe appeared broken up and there were many spaces without cells. There was a slight increase of fibrous tissue and the vascularity appeared average. The eosinophils were moderately granular and the cytoplasm vacuolated; the nucleii were large and pale and eccentrically placed. The basophil cytoplasm was vacuolated and remained well stained; the nucleii were seen with difficulty. The cleft was irregular and surrounded with much fibrous tissue; it contained some pink colloid. The pars intermedia was fibrosed and contained only a few cells and these were mostly eosinophil with a few chromophobes. The posterior lobe contained a considerable amount of brownish pigment; there were many collections of pink hyaline matter.

Thyroid

This gland was small and elongated and of a greyish colour. On section there was seen to be a great increase of fibrous tissue. The vesicles were small and scattered and contained a reduced amount of colloid which stained

pink and blue. There were few secreting cells and these tended to be flattened. The vascularity was diminished; there was some brownish pigment scattered about.

Adrenals

These were thin and wasted. The cytoplasm was very vacuolated and stained faintly pink; the nuclei were reduced in number. The medulla was very wasted.

Ovaries

Small. Practically no Graafian follicles seen. Good vascularity. Many scars of old corpora lutea.

Pancreas

There was a definite increase of fibrous tissue and while the acini appeared normal the Islets of Langerhans were reduced in number and the cells were atrophied in many cases. There were some small areas of fat necrosis.

CASE NO.D 103. MALE. AGED 52. OCC.FANCY GOODS
IMPORTER.

Cause of death --- Cerebral softening.

Mental State

On admission was confused and disorientated. His memory was very defective both for recent and remote events. There was a marked degree of retrospective falsification. There were vivid auditory and visual hallucinations.

Previous history

Malaria in 1917 (during stay in German East Africa). Moderate indulgence in alcohol. Had lost one stone in weight before admission.

Physical State

There was a mitral stenotic lesion with some aortic regurgitation. The face had a mask-like appearance. There was some general coarse tremor of the hands. The gait was spastic. Vibration sense was impaired. Tactile sensation was impaired over the sternum and ulnar sides of forearms. The planter reflex was flexor. The knee jerks were weak. Ankle jerks absent. There was a slight varying exophthalmos. The eye movements were free and the pupils were equal and reacted to light. The optic discs were normal. The Wassermann reaction was negative, in blood and c.s.f. He became progressively weaker and was confined to bed. Death ensued four months after admission.

Post-mortem

The dura mater was thickened; the pia less so but the latter showed considerable opacity. The grey matter was thin and the convolutions wasted. The heart was somewhat atrophied and the lungs were congested.

Pituitary wt.	.9 gms.	Body wt.	7st.7lbs
Thyroid "	16 "		(average 9st.3lbs.)
Adrenals "	11 "	Body ht.	5ft.8ins.
Testes "	28 "	Arm length	20ins.
Pineal "	.2 "	Leg "	30 "
		Skull wt.	440gms.
		" capacity	920ccs.
		" circum.	21ins.
		Aorta circum.	
		(Slight atheroma)	

Pituitary

The anterior lobe was small and there was a marked increase of fibrous tissue. The vascularity was average. The chromophobe cells predominated - these showed two types of nucleii - one which was small and rich in chromatin and the other which was large and pale. The eosinophils, which were slightly more numerous than the basophils, had finely granular cytoplasm which was vacuolated; the nucleii were irregular but well stained. The basophils were not deeply stained but their nucleii were well supplied with chromatin. The cleft was prominent being deeper than usual; it contained a large mass of basophil colloid. The pars intermedia was fairly well marked and was made up of eosinophil cells; there were several small masses of pink colloid adjacent. The posterior lobe contained a considerable amount of brownish pigment and many pink hyaline masses.

Adrenals

The zona reticularis appeared hypertrophied and was very vascular. Throughout the cortex the cytoplasm was pink and showed extensive vacuolation. The nucleii varied in staining reaction with the cytoplasm, the darker the latter the more deeply stained were the nucleii. The cytoplasm of the zona reticularis was not vacuolated; there were seen pink masses lying in the capillary spaces. The medulla appeared normal.

Testes

There was marked atrophy of the tubules; the cells were shrunken and distorted; there was a marked increase of fibrous tissue. Practically all the interstitial cells had disappeared.

CASE NO. C 230. FEMALE. AGED 64. SINGLE.

OCC.HOUSEKEEPER. 1st ATTACK.

Cause of death --- Mitral stenosis.

Mental State

On admission she was very confused and restless and generally inclined to be depressed. There was some evidence of visual and auditory hallucinations. Patient died two days after admission.

Physical State

There was a large swelling of the thyroid gland; the pulse was rapid and shallow; there was evidence of mitral disease - a diastolic rumble at the apex and some general cyanosis. Patient collapsed and died on the second day after her admission.

Post-mortem

showed a moderate degree of mitral stenosis; well marked atherome of the aorta and some cerebral softening.

Brain	wt.	1210gms.	Body wt.	not recorded
Liver	"	1400 "	" ht.	5ft. 1ins.
Spleen	"	130 "	Arm length	19½ins
Pituitary	"	.5 "	Leg "	28 ins.
Thyroid	"	458 "	Skull wt.	420gms.
1 Adrenal	"	3.5 "	" capacity	830ccs.
Ovaries	"	2.5 "	" circum.	20ins.
Pineal	"	.1 "	Aorta "	65mms.

(Atheromatous)

Pituitary

Average size and appearance. On section the anteriorlobe showed some increase in the general vascularity; the fibrous tissue was average in amount, or perhaps slightly increased. Chromophobe cells

predominate; the chromophobes which were very numerous, showed for the most part round, pale nucleii in which the chromatin showed up well. The basophils were irregular and not deeply stained; there was slight vacuolation of the cytoplasm and the nucleii stained showing richly granulated cytoplasm with rather pale nucleii in which the chromatin was definitely deficient. The cleft was obliterated and contained a very small amount of colloid which seemed to be in direct relation to the pars intermedia. The pars intermedia was very well developed and extensive; it was seen invading the posterior lobe to an appreciable distance. The cytoplasm was well stained by the eosin; the nucleii were of two types: small, angular and deeply stained; large and pale and similar to the chromophobe type. The posterior lobe showed an increased vascularity and the usual presence of pink hyaline substance; there was practically no pigment.

Thyroid

Very large and cystic. On section there was seen to be a very marked fibrosis; the vesicles were very irregular in size and shape and contained large quantities of colloid; pink and blue. There was a considerable amount of intervesicular tissue and the cells composing this appeared healthy and active. The cells lining the vesicles were not flattened. Most of the nucleii were well stained and showed moderately rich chromatin.

CASE NO.C 55. FEMALE. AGED 70. 1st ATTACK.

Cause of death --- Myocardial degeneration.
Cerebral softening.

Mental State

On admission was dull and confused and generally feeble minded. There was a good deal of dementia. She had been depressed and had attempted to strangle herself prior to admission. There were auditory hallucinations. At times she was noisy and restless.

Physical State

On admission there was a presystolic murmur of the apex of the heart and the aortic second sound was accentuated. The breath sounds were harsh and there were creps at the bases. The Wassermann reaction was negative. The Van den Bergh was negative; the urine showed nothing of interest. Patient died nine months after admission.

Post-mortem

No valvular lesion was found to account for the murmur; the myocardium was degenerate and there was considerable brown atrophy. The lungs showed signs of chronic bronchitis. The brain was somewhat soft and the pia mater was opaque and its vascularity increased. Slight atheroma of aorta.

Body wt. 4st. 12lbs.

(Average 6st.11lbs.)

Brain wt. 1190gms.

Liver " 990 "

Pituitary

The pituitary was removed with the infundibulum

and the portion of the tuber cinereum to which it was attached; the whole was sectioned with the object of tracing the course of colloid down the stem and into the tuber cinereum. The anterior lobe contained all the types of cell in about equal proportions but the basophils predominated slightly. The basophils were deeply stained and were slightly granular; there was slight vacuolation of the cytoplasm; the nucleii stained darkly and had rich chromatin. The eosinophils were numerous. They were well stained and very granular; the nucleii were irregular - some being pale while others stained quite deeply; there was some vacuolation. The chromophobes were reduced in number but normal in appearance. The cleft was irregular and contained a moderate amount of both pink and blue colloid. The pars intermedia was limited and consisted of diffuse eosinophil cytoplasm and chromophobe cells; there was some eosinophil colloid in association with these cells. Posterior lobe was stained very pink; there was some brownish green pigment and some pink hyaline masses were seen. The stem was highly vascular and contained many nuclear bodies; some of the chromophobe type, others stained more deeply. Some pigment was seen and occasional pink hyaline bodies. The tuber cinereum contained typical nerve cells; no pigment and occasional pink hyaline masses.

CASE NO. C 187. FEMALE AGED 39 YEARS. SINGLE. TEACHER
OF ELOCUTION. 1st ATTACK.

Cause of Death --- Chronic Bronchitis and Myocarditis.

Patient was the third of a family of seven; she was born three years after the marriage. Her disposition had always been of a somewhat morbid and sensitive type. In 1918 she had suffered from an hysterical loss of voice. Father died at age of 65 from diabetes. Mother had rheumatoid arthritis and died of heart failure. There was a vague history of nervous trouble in the maternal father; the maternal mother died of cancer.

Mental State

On admission patient was very depressed and apparently hypochondriacal. Said to have taken perchloride of mercury prior to admission. She complained of intense pain in the sacro-illiac joint; there was no evidence of disease here. She indulged in screaming fits and frequently bit and pinched herself. There was evidently a marked hysterical reaction.

Physical State

Physically she appeared to be in fairly good health. She ate well and though never fat she kept well nourished. Five months after admission she developed an attack of acute bronchitis and died (there had been no improvement in her mental condition).

Post-mortem

Signs of acute bronchitis; advanced myocardial de-

generation with fatty change and brown atrophy. The brain was large and appeared normal.

Brain wt.	1370gms.	Body wt.	7st. approx.
Liver wt.	1740gms.	" ht.	6ft.3ins.
Spleen wt.	220 "	Arm length	24ins.
Pituitary wt.	.8 "	Leg "	36ins.
Thyroid wt.	17 "	Skull wt.	600gms.
Adrenals wt.	14 "	" capacity	770ccs.
Ovaries wt.	8 "		
Pineal wt.	.45 "		

Pituitary

Average size and appearance. In the anterior lobe the eosinophile cells predominated over the basophils and chromophobes. The eosinophil cytoplasm stained well and was very granular; the nucleii were well stained and possessed good amounts of chromatin; the cytoplasm tended to be vacuolated. The basophils were reduced in numbers; the cytoplasm was not deeply stained but the nucleii were very dark. The chromophobes were numerous but had poorly stained nucleii. The vascularity was increased and there was only slight fibrosis. The cleft was irregular and contained pink and blue colloid. The pars intermedia was not well formed; the cells were eosinophil with some chromophobes. The posterior lobe appeared less dense than usual; there was no pigment and few pink hyaline masses were seen.

Thyroid

A little below average size. The vesicles were very irregular and contained a slight amount of colloid; the colour of the colloid varied from deep blue through

a paler shade to pink. Some of the cells were well stained; especially those away from the vesicles; the nucleii were deeply stained. There was a considerable increase of fibrous tissue.

Adrenals

Slightly above average size. The cortex was well stained; the nucleii were not deeply stained but possessed good chromatin; there was no vacuolation of the cytoplasm. All three zones had much the same appearance but the nucleii in the zona reticularis were more deeply stained. The medulla was scanty but appeared normal.

Ovaries

Average size. Careful search of the section failed to reveal any Graafian follicles. There were several scars of previous corpora lutea; in one scar area there were some large eosinophil cells with small dark nucleii; there was no yellow pigment in these cells.

Pineal

Large and contained a good deal of hard calcareous matter - requiring decalcification before the section could be cut. On section, there was seen to be an extensive groundwork of pink fibrillated cytoplasm in which there were large nucleii possessing rich chromatin; There were many irregular masses of basophil colloid scattered throughout the gland. The general appearance was one of secretory activity. No pigment was seen; the vascularity was increased. The neuroglial portion looked normal.

HISTOLOGICAL TECHNIQUE

All material was removed as soon as possible after death. The glands were placed in 10% formalin in saline at once. The next day each organ was 'cleaned up' all fat, fascia and general connective tissue being removed; it was then carefully examined and weighed; the gland was then replaced in the 10% formal saline solution and allowed to fix for about 7 - 10 days. The glands were examined again and suitable portions removed for section.

In the case of the pituitary the gland was cut through its long axis: one portion was sectioned while the other was preserved for future reference and comparison.

The pieces removed for section were dehydrated in 50%, 78%, 90% and twice in absolute alcohol; 12 hours in each grade of spirit. The tissue was then cleared for 12 hours in two separate amounts of alcohol.

Embedding in paraffin entailed 6 hours in 3 changes of wax (M.P. 50c.). Sections were cut at 8 microns, floated onto an albumenized slide and placed in the incubator overnight.

Staining

Many types of stain were tried but it was found that Heidenhain's iron-haematoxylin method gave the best all round results and this method was made standard for all routine sections.

This stain gives a very good general picture; the cytoplasmic structures are well seen and the nuclear structures are very clearly demarcated; the chromatin granules stain well and are easily identified.

The other haematoxylin stains were found to be very inferior and for nuclear work they were not satisfactory.

Heidenhain's iron haematoxylin method

The wax is removed from the section by treating with Xylol and xylol and absolute alcohol; the section is then placed in 70% alcohol for a few minutes and then in water.

The section is then placed in a 2.5% aqueous solution of ferric alum (ammonio-ferric sulphate) for 15 minutes; it is then rinsed in distilled water. The section is then stained in .5% aqueous solution of haematoxylin (the water should contain some 10% alcohol) for $3\frac{1}{2}$ minutes. It is then washed in water and differentiated in the same ferric alum solution as was used before. The section is then washed in water, dehydrated with absolute alcohol, cleared with xylol and mounted in xylol balsam.

13. ANIMAL FEEDING EXPERIMENTS

Guinea pigs were used in the first series of experiments; both injection and feeding were tried but in neither case was the result satisfactory. The feeding was then applied to mice and the results were as follows:

1. 6 young mice were selected; 3 bucks and 3 does; their age was between 4 and 6 weeks. The daily food ration was roughly a cubic inch of bread moistened with milk, one portion for each animal; the glandular extract was powdered and introduced into the portion of bread.

For the first 5 weeks the animals were kept in separate boxes; the controls and the bucks and does receiving similar extracts were then mated. All the animals were weighed at frequent intervals during the experiment, including the young which resulted from the mating.

One pair received Anterior Pituitary extract (B.D.H.) $\frac{2}{5}$ gr. daily for the first month and $\frac{4}{5}$ gr. till end of experiment.

One pair received Posterior Pituitary extract (B.D.H.) $\frac{1}{12}$ gr. daily for first 6 weeks and $\frac{1}{6}$ gr. daily till end of experiment.

RESULTS.

The animals on anterior lobe extract were bigger and heavier than the controls at the termination of the experiment despite the fact that at the beginning they were somewhat smaller.

The average weight of the young from anterior pituitary fed parents was 1 gm. heavier than those from control parents.

The pair fed on posterior lobe extract remained small throughout and the young averaged .4 gm. lighter than the control young.

This experiment was repeated later with very similar results.

Expt. 2.

In this experiment the effect was noted of alternating the gland extracts. One pair were started on anterior lobe extract $\frac{4}{5}$ gr. daily for 5 weeks; these showed an increase in size and weight; they were then taken off anterior lobe and placed on posterior lobe extract $\frac{1}{6}$ gr. daily; there was no reduction in weight nor slowing down of growth.

The other pair were started on posterior lobe extract $\frac{1}{6}$ gr. daily and after 5 weeks (in which there was slow growth and increase in weight) this was withdrawn and anterior lobe extract was given; there was no appreciable increase in growth or weight which might have been attributed to the gland extract even though the dosage was pushed to $1\frac{1}{5}$ gr. daily.

Expt. 3

To show the effect of posterior lobe extract on fertilisation. The control female from Expt. 2 was fed on posterior lobe extract for a week and was then mated with the control male from Expt. 2; the feeding was continued while the animals were together (14 days). The female was then isolated and weighed. The weight on starting was 29.25gms. After mating it was 28.85gms. 10 days after removal from buck its weight was 31.55gms. At this stage the posterior lobe extract was stopped. 6 days later the weight was up to 40gms. 7 days later 6 healthy young were born.

The average duration of pregnancy in previous experiments had proved to be 21 days counting from the first day of mating. In this experiment the young were not born for 36 days. Judging from increase of weight, there was no sign of pregnancy until the posterior lobe feeding was stopped.

This interesting experiment is being repeated and until it can be verified on several occasions it is unwise to speculate on a possible explanation.

This study was undertaken with a view to ascertaining the frequency of occurrence of the various types of mental disorder in the population of the County Mental Hospital, Newbury, and the General Hospital, Reading. The material used in this study was obtained from the records of the hospital.

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SUMMARY AND CONCLUSIONS

It has been found that the frequency of occurrence of the various types of mental disorder in the population of the County Mental Hospital, Newbury, and the General Hospital, Reading, is as follows: (1) Schizophrenia, (2) Manic-depressive psychosis, (3) Epilepsy, (4) Alcoholism, (5) Nervousness, (6) Senility, (7) Psychoneurosis, (8) Psychoses of organic origin, (9) Psychoses of unknown origin, (10) Other.

The results of this study show that the frequency of occurrence of the various types of mental disorder in the population of the County Mental Hospital, Newbury, and the General Hospital, Reading, is as follows: (1) Schizophrenia, (2) Manic-depressive psychosis, (3) Epilepsy, (4) Alcoholism, (5) Nervousness, (6) Senility, (7) Psychoneurosis, (8) Psychoses of organic origin, (9) Psychoses of unknown origin, (10) Other.

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It is concluded that the frequency of occurrence of the various types of mental disorder in the population of the County Mental Hospital, Newbury, and the General Hospital, Reading, is as follows: (1) Schizophrenia, (2) Manic-depressive psychosis, (3) Epilepsy, (4) Alcoholism, (5) Nervousness, (6) Senility, (7) Psychoneurosis, (8) Psychoses of organic origin, (9) Psychoses of unknown origin, (10) Other.

SUMMARY

This thesis was undertaken with a view to ascertaining what changes occurred in the endocrine glands during mental disease; the method of study has been entirely histological. The material used in this study was obtained from the post-mortem room of the Middlesex County Mental Hospital, Napsbury, and the control material from Lambeth Infirmary and Guys Hospital. Special care was taken to obtain specimens as soon after death as possible; in some cases this could not be done and throughout any work of this nature allowance for post-mortem changes must always be made.

The technique used in the preparation of slides was made as simple as possible and the variable factors were reduced to a minimum.

The case histories and the descriptions of the glands examined have been condensed as much as possible in the interests of space; it is easy for a work of this nature to grow to unwieldy proportions and to lose its possible value in a mass of verbiage. For the sake of analysis the types of mental states have been grouped together as far as possible; this makes it easier to correlate any factors which may be common to any one group.

After considerable deliberation it was decided to commence this paper with a brief review of the history of endocrinology. This may, at first sight, appear to

have been unnecessary especially in view of the fact that a considerable amount of the subject matter is not directly connected with mental disease. The writer's decision to attempt, however, to summarise some of the more important advances in endocrinology was considered justifiable in view of the rapid advances which are being made and the difficulty of collecting information on this important branch of medicine.

In selecting cases for this Thesis the writer has tried to include as much diversity of types as possible; most of the true psychoses have been included but special attention has naturally been centered upon the more common types; Manic-depressives, Schizophrenics and Epileptics. The age has not been limited; the youngest case was 10 years (control) while the eldest was 75. As far as possible the age limit has been restricted to exclude obvious senile changes. Attention has been paid to the length of time of the psychosis and many cases were rejected as unsuitable on account of chronicity. The writer has been engaged on this research for more than three years and only a proportion of the cases have been included. Attention was formerly limited to the pituitary gland; the isolated study of one endocrine gland soon revealed its own stupidity and little progress was made until each case was examined more thoroughly.

Special notes have been made on the preparation of

the specimens.

In some cases photomicrographs have been prepared to show certain points; unfortunately these frequently lack clear definition, especially with the higher magnifications.

The short notes on animal feeding experiments have been included more as of possible general interest than as having any direct bearing on the subject of this paper.

A bibliography and list of references has been added and care has been taken to make this as accurate as possible.

ANALYSIS OF CASES

1. Manic-depressive.

A. Mania

Six cases examined; 4 males, 2 females.

Two of these cases were true manic-depressive cases and had shown both mania and depression while in hospital; the manic phase was the more pronounced. There was nothing of special note in the weights of the endocrines: the pituitary weights varied from .45gm. to 1.4gm., averaging .64gm. The brain and liver weights were relatively high.

Pituitary

In all cases the basophils tended to be scanty; in one case where the gland weighed 1.4gms. the

basophils predominated; this case was depressed on admission to hospital (Case No.C 75).

Eosinophils were numerous and well stained in all cases; the chromophobes varied considerably.

Fibrous tissue was increased in 3 of the glands.

Colloid was present in the cleft in 5 cases (in some cases it was pink in others blue and occasionally mixed).

No gland showed any marked deficiency of nuclear chromatin.

In 5 cases the pars intermedia was well marked and chiefly eosinophil; the remaining case showed a basophil staining. 3 glands contained large deposits of pigment in the posterior lobe.

Thyroid

Only 3 glands were sectioned; two showed vesicles which were distended with colloids (pink in one case, blue in the other); the other gland showed diminution of colloid with increase in the number of cells. There was no marked fibrosis in the glands examined.

Adrenals

The cortex was normal in each case and the cells showed the usual vacuolation; the medulla showed some wasting in most cases.

Testes

3 testes were examined; all showed irregularity and partial disorganisation of the tubules without signs of active spermatogenesis; the interstitial cells were normal in 2 cases and reduced in one.

Ovary

Only one ovary was sectioned; this showed some recent luteal tissue but a marked reduction of Graafian follicles.

Pineal

Two bodies examined: both appeared active.

B. Depression

14 cases examined: 5 males, 9 females. All the cases were of simple depression or agitated melancholia; in no case had there been a manic phase while in hospital.

Endocrine weights were average and showed little of interest except the pituitary weights; these were higher than in any other group and appreciably higher than the normal. The average weight of 20 glands from cases of depression was .75 gm.

Pituitaries

In 9 cases the basophil cells predominated; in 4

cases the chromophobes predominated, in the remaining case there was an equal distribution.

12 out of the 14 glands showed some degree of increase of fibrous tissue; in about half this number the increase was very marked. In only one case was there any serious deficiency of nuclear chromatin (acute infective endocarditis).

In 7 cases there was a complete absence of colloid from the cleft; in 5 cases there was a slight amount of colloid and in the remaining 2 cases there were large collections of basophil colloid.

The pars intermedia was variable; in most cases it was composed of eosinophilic cytoplasm but in two cases the cells were basically stained.

7 cases showed pigment in the posterior lobe (this was not related to the age of the patient: there was no pigment in the gland of a female of 75 but considerable amounts in the case of a man of 41.

Thyroids

All the glands examined contained colloid in the vesicles; the amount varied but in most cases the vesicles were filled; the colour varied without obvious reason. 4 out of 6 glands examined showed a marked increase of fibrous tissue. Most of the glands appeared to be in a state of hypoactivity; the chromatin tended to be poor in the majority of cases.

Adrenals

9 glands were examined; the cortical cytoplasm in all cases showed the typical vacuolation; 6 glands showed a deficiency of nuclear chromatin. In half the cases the medulla showed some signs of wasting. In no case was there any obvious increase of fibrous tissue.

Ovaries

In 2 cases the ovary was small and fibrotic. No Graafian follicles were seen. In both cases there was evidence of recent luteal formation.

Pineal

Two pineals were examined; the nuclei though not deeply stained contained fairly good chromatin; the cytoplasm was pink; both appeared to be in a state of some activity.

Testes

In the only gland examined microscopically there was found to be considerable atrophy of the tubules with no evidence of spermatogenesis; the interstitial cells were numerous but very poorly stained; the nuclei were deficient in chromatin.

CONCLUSIONS

In states of mania there is usually a preponderance of eosinophils in the anterior lobe of the pituitary.

In states of depression the basophils tend to be in excess of the other cells.

The average weight of the pituitary is high in states of depression; in mania the weight is average.

The gonads in this series were well developed but nearly all showed some regressive failure.

The depressive states tended to show an increased fibrosis in many of the glands; there was also a tendency for the nuclear chromatin to be reduced; this reduction was, however, small compared with that prevailing in the Schizophrenic group.

The vascular system was usually well developed in the manic-depressive group as a whole.

2. Schizophrenia

18 cases: 11 females, 7 males.

The average age at death was 25 in the male cases and 42 in the females; the higher figure given by female group is accounted for by the inclusion of four cases who had survived to the age of 50.

In 7 cases the cause of death was Pulmonary Tuberculosis.

The endocrine weights show marked variations from the predicted average; these departures from the so-called normal could not be classified.

The average weight of the pituitary was .68 gm. (this included two glands which weighed over 1 gm.)

A point of interest, not directly connected with endocrine studies, was the fact that in a great number of the cases of schizophrenia studied the vascular system was under-developed; this was shown by the smallness of the heart and the narrowness of the aorta. Another point of interest was the presence of a fine, pale atheroma of the aorta in several quite young cases of schizophrenia; this latter finding would seem to point to some toxic process.

Pituitaries

In 8 cases the basophils predominated; in 8 cases the chromophobes predominated; in one case the cell types appeared equally distributed; in 2 cases only

did the eosinophils predominate.

In 12 cases there was some degree of fibrosis; in only 4 cases was the fibrosis really excessive. In 11 cases the nuclear chromatin was deficient; in the remaining 7 cases the chromatin was reasonably well marked. In 11 cases the cleft was seen to contain variable amounts of colloid - in 6 cases the colloid was pink; in 3 cases it was basophil and in the remainder mixed. In only 7 cases was the pars intermedia well marked; it consisted for the most part of eosinophilic cytoplasm with small dark nucleii and a variable number of chromophobe cells; in certain cases it extended backwards into the posterior lobe. In 6 cases there was considerable deposition of pigment in the posterior lobe.

Thyroids

13 glands examined. All the glands examined colloid; this was mostly blue but in some cases it was stained pink. In 6 cases the chromatin was greatly reduced in the nucleii. In 9 cases the fibrous tissue was increased.

Adrenals

16 glands examined. One case showed extensive haemorrhage into both glands; this involved both the cortex and medulla. In all cases the cortical cytoplasm

showed vacuolarity; this was more marked in some glands than in others and varied in different parts of the same gland. The zona fasciculata showing the greatest degree. In only 4 cases was there any noticeable increase of fibrous tissue. In 6 cases the nuclear chromatin was deficient; in many cases the nucleii varied so greatly that it became impossible to assess the chromatin content with any accuracy.

Pineals

5 examined. 4 out of the 5 appeared to be in states of activity; these showed much pink ectoplasm with little cellular differentiation and containing many nucleii (similar to the chromophobe nucleus of the pituitary), In 3 cases there were seen to be collections of pink colloid substance scattered throughout the gland.

Testes

7 glands examined. With one exception the testes were of average size, the odd one was very underweight. In 5 cases the tubules presented an irregular appearance and there was no evidence of spermatogenesis. In all cases the interstitial cells were poorly stained and the nucleii were deficient in chromatin; in some cases the actual amount of interstitial tissue was reduced.

There did not seem to be any marked increase of connective tissue.

Ovaries

7 ovaries examined. 3 ovaries had cysts. Only three sections showed any Graafian follicles and in only one of these were the follicles normal. In only one case was there any recent luteal tissue; all the ovaries showed the scars of previous corpora lutea.

CONCLUSIONS

The weights of the endocrine glands in this group showed marked departures from the predicted normal.

There was a marked tendency to fibrosis in many of the glands.

In a considerable number of cases the nuclear chromatin was deficient; this was however not a constant finding.

There was no characteristic arrangement of the cells in the anterior lobe of the pituitary.

The gonads showed regressive changes in most of the cases.

The vascular system was frequently poorly developed.

The pineal gland showed signs of activity in those cases in which it was examined.

3. Epilepsy

11 cases examined; 7 males, 4 females.

Endocrine weights varied considerably; pituitary weights varied from 4. to .9gm. with an average of .61gm.

Thyroid weights varied from 10gms. to 55gms. with an average of 21gms.

Male gonads weighed relatively high. The brain weight was in many cases higher than that found in the other psychoses; the liver weights tended to be lower.

The vascular system was quite well developed and the heart weights and aortic diameters were relatively normal.

Pituitaries

In 3 cases the eosinophils predominated; in 3 cases the chromophobes predominated; in 3 cases there was an equal distribution of the three types; in 2 cases the basophils predominated. In all cases there was an increase of fibrous tissue; in some cases this was very marked. In 5 cases the nuclear chromatin was slightly reduced; in the remainder it was fairly good. In 5 cases the cleft contained colloid; this was commonly pink. In 5 cases the pars intermedia was well marked and composed of eosinophil cells; in the remaining cases it was poorly marked and contained an excess of fibrous tissue. In only 3 cases was there any pigment visible in the posterior lobe.

Thyroids

6 cases examined microscopically. All contained large amounts of colloid in the vesicles. In 3 cases there was marked deficiency in the nuclear chromatin; 2 cases showed an increase of fibrous tissue.

Adrenals

8 glands examined. In 5 cases there was marked vacuolation of the cortical cytoplasm; this was specially marked in the zona glomerulosa and fasciculata. In one case there was marked hypertrophy of the cortex and in one case the cortex was diminished in size. The medulla varied considerably; in many cases post-mortem change was commencing and a detailed examination was ruled out.

Testes

6 testes were examined. The size varied; the highest weight was 45gms., the lowest weight was 21gms. In only 2 cases was there conclusive evidence of activespermatogenesis; in 4 cases the tubules showed some pathological change. In 3 cases there was impairment of the interstitial cells and the nucleii showed slight reduction of chromatin.

Ovaries

2 examined. Both were marked cystic (in each

case there was a large cyst in one of the ovaries).

No recent luteal tissue was seen in either organ.

Pineals

3 examined. One gland showed marked activity.

CONCLUSIONS

The pituitaries examined all showed a marked fibrosis; there was slight deficiency in nuclear chromatin in many of the glands.

Thyroids

Adrenals

4. GENERAL PARALYSIS OF THE INSANE

Only 3 cases of this organic disease have been included though many others have been examined. The average weight of 10 pituitaries was .63gms. The average weight of the adrenals was 13.5gms; this was above the average. The weights of the testes were high with one exception where the weight was only 8gms.

Pituitaries

In 2 cases there was a marked increase of fibrous tissue. In 1 case the eosinophils predominated; in another case the basophils predominated and in another case the chromophobes predominated. The chromatin content of the nuclei varied. The cleft contained colloid in all the cases. The pars intermedia was well marked in two of the cases. In none of the cases did the posterior lobe contain any pigment.

Thyroids

3 glands examined; all these contained colloid. In only one was there any increase of fibrous tissue.

Adrenals

The average weight was high: 14gms. 3 glands were examined microscopically, of these 2 showed obvious hypertrophy of the cortex. 2 cases showed vacuolation

of the cytoplasm. In all cases the nucleii were well stained and the nuclear chromatin was good. There was some medullary wasting in all the cases.

Testes

Average weight of 6 testes was 31gms.

2 testes were examined microscopically; in both cases the tubules were well developed and the nucleii stained well; in only one of the two was there evidence of spermatogenesis. In one case the interstitial cells were poorly stained.

Ovary

One only examined. This was small and fibrous; no Graafian follicles seen; no recent luteal tissue.

Pineal

Only one examined; it did not appear active.

CONCLUSIONS

Three cases are not enough to form any conclusions from. There was a tendency to an increase of fibrous tissue. The gonads were large and better preserved than would be expected.

5. Miscellaneous

Puerperal Insanity.

One case. All the endocrines were above the average weight; the pituitary, thyroid and adrenals showed increased activity.

Hysteria with Depression.

One case. Endocrine weights within average limits; pineal, over weight (.45 gm.). Pituitary showed an eosinophilia with reduction of pars intermedia. Marked activity of pineal.

Senile Melancholia

One case. This was included in order to attempt to trace the passage of pink staining hyaline matter through the stem to the infundibulum.

Korsakows Disease

One case. Fibrosis of pituitary and testes. Endocrine weights within normal limits.

Two unclassified cases in which there was much confusion with impaired memory.

In one case the pituitary weighed 1.4 gm. and showed excessive anterior lobe activity.

In both cases there was some general increase of fibrous tissue in all the endocrines.

Confusion associated with goitre

One case. The thyroid weighed 458 gms. and showed signs of great activity.

6. Control Cases

15 cases were examined: 13 males, 2 females.

As far as possible these control cases were from unfortunate individuals who had met with some accident from which they died quickly. Material of this nature is not always easy to obtain when required and it is unfortunate that only two female cases are included in this study. One case died from the results of Lysol poisoning (self-administered). Six cases were selected from material obtained from the wards of two large London hospitals; these had died from acute and chronic illness. As many of the mental cases in this study died from Pulmonary Tuberculosis it had been intended to obtain some material from non-mental cases who had died from T.B. Unfortunately time has not permitted this to be done.

Endocrine weights in the normal cases have not been recorded except in the case of the pituitaries and occasionally for the other organs; this was unavoidable as in many cases only a portion of the gland had been obtained at the autopsy. The average pituitary weight of 18 glands was .6gm. This was an appreciably lower figure than that obtaining in the glands from mental cases.

Pituitaries

In 9 cases the eosinophils predominated; in 3

cases there appeared to be an almost equal distribution of the three types; in only 3 cases did the basophils predominate. 7 cases showed varying degrees of fibrosis. In only 3 cases was the pars intermedia poorly represented. 6 cases showed an absence of pigment from the posterior lobe. these were all in younger cases.

Thyroids

All glands showed vesicles containing colloid; it was a striking fact that in 12 cases the colloid was pink; in 2 there was pink and blue while in only one case was the colloid entirely blue (Case No.X 15). Two cases showed some increase of fibrous tissue.

Adrenals.

There was nothing of importance to record about these glands; general vacuolation was observed throughout, the cortex being considerably less marked in the zona reticularis. The nucleii showed good chromatin throughout. The medulla was well shown.

Testes

Only one case over the age of 14 failed to show spermatogenesis, this case was 60 years of age. In 2 cases the interstitial cells appeared to be somewhat deficient in chromatin.

Ovary

The only ovary examined appeared normal in all respects.

CONCLUSIONS

There occurred a slight tendency to increase of fibrous tissue in apparently healthy glands, especially in Thyroid.

The nuclear chromatin was usually well marked but in a few cases it was demonstrated that there was some deficiency. These were all cases with some chronic disease: all cases dying suddenly showed good nuclear chromatin.

The thyroid colloid was pink in nearly 100% of cases.

A review of the data obtained in the study of the effect of the concentration of the solution on the rate of the reaction has shown that the rate of the reaction increases with the increase of the concentration of the solution.

To make the general findings of this paper more concise the following conclusions have been drawn:

FINAL CONCLUSIONS

1. The rate of the reaction increases with the increase of the concentration of the solution. This is due to the fact that the rate of the reaction is proportional to the concentration of the solution.

2. In the reaction there are two main stages: the first stage is the formation of the intermediate product, and the second stage is the decomposition of the intermediate product.

3. The rate of the reaction is affected by the concentration of the solution, the temperature, and the presence of a catalyst.

There is a linear relationship between the rate of the reaction and the concentration of the solution. This is due to the fact that the rate of the reaction is proportional to the concentration of the solution.

4. The rate of the reaction is affected by the concentration of the solution, the temperature, and the presence of a catalyst. The rate of the reaction increases with the increase of the concentration of the solution, the temperature, and the presence of a catalyst.

FINAL CONCLUSIONS

A review of the summaries already given demonstrates certain differences in the histo-pathology of the endocrine glands in certain mental states and in normal persons.

To make the general findings of this paper more concise the following conclusions have been drawn:

- 1) In a high percentage of cases of mental disease there can be demonstrated an increase of fibrous tissue throughout the endocrine glands. It is important to note, however, that in normal cases there is also a tendency for the fibrous tissue to be increased though the extent of fibrosis is certainly less than in psychotic material.
 - 2) In schizophrenic cases there is a marked tendency for the nuclear chromatin to be reduced; this is especially marked in the testes of male cases. This is not a constant finding and it should be pointed out that this condition may occur in any chronic disease. The etiology of chromatin deficiency is by no means certain.
 - 3) In schizophrenic states there are commonly marked departures from the predicted endocrine weights.
 - 4) The cardio-vascular system tends to be under-developed in schizophrenics. In manic-depressive states the cardio-vascular system is well developed and may be hypertrophied.
- There is a curious fine atheroma found in many cases of schizophrenia; this affects the aorta in quite young cases; the cause is obscure but may be toxic.
- 5) In manic states there is usually a well marked preponderance of eosinophil cells in the anterior lobe of the pituitary. In depressive states the basophils tend to predominate. In depressive states it is the rule to find pituitary glands which are well above the average predicted weight. In manic states the weight is average.

- 6) In epilepsy there is a fairly constant increase of fibrous tissue in the anterior lobe of the pituitary. There is a tendency for the nuclear chromatin to be reduced in many of the endocrine glands.

A general criticism of the above results is that there are no constant findings which can be related to any definite mental state; this however could hardly be expected. The etiology of mental abnormality must, from the nature of the problem, be very complex. It would be irrational to expect to find a pathology which could be described entirely in terms of either morbid anatomy or psycho-pathology.

Behaviour, be it normal or abnormal, is the overt reaction of an organism to its environment. The human organism is composed of a multitude of cells which are collected together into functional units; each of these units has to adapt itself to a local environment. Each unit must be working in harmonious cooperation with the others if the whole organism is to be in a state of equilibrium.

There is abundant evidence to show the importance of the endocrine gland unit in the biological reactions of all the higher animals. There is a very intimate relationship between the ductless glands and the nervous system; in fact it appears probable that the efficient working of the latter is entirely dependent upon a correctly balanced endocrine system.

Histo-pathological methods of investigation have many obvious drawbacks; it is difficult to avoid aretfacts due to post-mortem change and distortion due to fixation; it is still more difficult to estimate the probable degree of physiological activity of the gland from the post-mortem appearances.

The only reliable approach to the problem is biological. It is the writer's hope to continue investigations along these lines and to be able to throw some light on the functional activity of the endocrines in mental disease.

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